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Review

Levels and profiles of persistent organic pollutants in breast milk in China and their potential health risks to breastfed infants: A review

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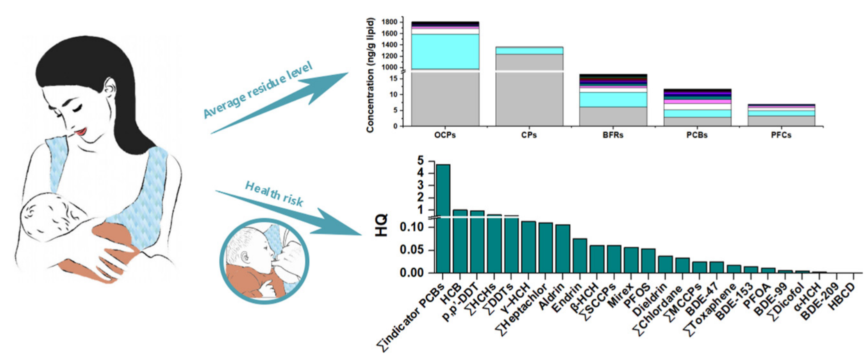
HIGHLIGHTS

- Levels and profiles of POPs in breast milk in China were reviewed.
- p,p'-DDE and short-chain chlorinated paraffins are the dominant pollutants in breast milk.
- The levels of traditional POPs declined over time, especially p,p'-DDE and β-HCH.
- Women living in coastal areas, urban areas, and southern China have a high body burden of certain POPs.
- Infants cannot suffer of a potential health risk through breastfeeding other than DDT, HCB, and PCBs.

GRAPHICAL ABSTRACT



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ABSTRACT

Although some persistent organic pollutants (POPs) were prohibited or limited in use several decades ago, they are still frequently detected in the human body. The purpose of this study was to understand the levels and profiles of POPs in breast milk in China and assess their potential health risks among breastfed infants under six months of age. A literature review focused on China was performed for studies published from 2001 to 2020. The POP levels in breast milk along with other important variables were extracted, and then the average individual POP levels in breast milk were estimated. This review summarises the distribution of traditional and new POPs, including polychlorinated biphenyls (PCBs), organochlorine pesticides (OCPs), legacy brominated flame retardants (BFRs), perfluorinated compounds (PFCs), and chlorinated paraffins (CPs) and reported notably high levels of short-chain chlorinated paraffins and 1,1-dichloro-2,2-bis (*p*-chlorophenyl) ethylene (p,p'-DDE) in breast milk. Although the levels of traditional POPs generally declined over time, especially p,p'-DDE and beta-hexachlorocyclohexane (β-HCH), women living in coastal areas, urban areas, and southern China still have a high body burden of certain POPs. In the present study, the estimated daily intake (EDI) of POPs through breastfeeding was used to evaluate the health risk for infants by comparing with acceptable levels. The findings suggested that infants born in coastal areas most likely suffered potential health risk from exposure to DDT, and the health risk of hexachlorobenzene (HCB) in infants in most nationwide regions remains a concern. More

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importantly, the EDI of PCBs for infants exceeds the safe limit on a national scale. Continuous surveillance of PCBs in breast milk is critical to evaluate the potential health effects on humans.

Contents

1. Introduction

Persistent organic pollutants (POPs) have been increasing concern due to their long-range transport, persistence, ease of accumulation in organisms, and potential toxic effects on humans and the environment. (Meng et al., 2017; Weber et al., 2019). POPs could biomagnify throughout the food chain and lead to high concentrations in top predators, including humans (Govaerts et al., 2018). Human exposure to POPs, even at the low exposure levels, have disruptive effects on the endocrine, reproductive, and immune systems, in addition to carcinogenic risk, neurotoxicity, and genotoxicity (Mostafalou, 2016; WHO, 2020). These issues were discussed at the Stockholm Convention in 2001 (UNEP, 2001), and finally a consensus was reached to reduce and eliminate the production and emission of POPs. At present, 28 chemicals are listed in the convention's annexes (UNEP, 2017), which were categorised into three categories, including pesticides, industrial chemicals, and by-products from unintentional production.

Although some POPs have been banned for several decades, they were frequently detected in the human body, such as maternal serum, cord blood, placenta, and breast milk (Li et al., 2020; Muller et al., 2019). For biomonitoring of POPs, breast milk is the preferred biological matrix compared to other samples because it is easily available, non-invasive, and efficient for the extraction of POPs (Acharya et al., 2019). In addition, strong correlations were observed between the concentrations in breast milk and maternal serum for polychlorinated biphenyls (PCBs) (Darnerud et al., 2010; Needham et al., 2011), Dichlorodiphenyltrichloroethanes (DDTs) (Muller et al., 2019), polybrominated diphenyl ethers (PBDEs) (Darnerud et al., 2015), and perfluorinated compounds (PFCs) (Fromme et al., 2010; Kim et al., 2011). The residue levels of POPs in breast milk may reflect the mother's body burden. The assessment of POPs in breast milk enables the estimation of dietary intake of breastfed infants, as has been widely reported for traditional and new POPs (Chan et al., 2007; Lee et al., 2018; Mamontova et al., 2017; Zhou and Yuan, 2020).

Breast milk is considered as a complete food for infants <6 months old, since it provides almost all of the essential nutrients and improves infant growth and development (Kishikawa and Kuroda, 2009). However, POPs, particularly highly lipophilic or low molecular weight, tend to accumulate in breast milk (Solomon and Weiss, 2002). Some lipophilic POPs can be transferred to infants through breastfeeding and have potential health risks in infants. For example, POP levels in breast milk were associated with infant gut microbial function (Iszatt et al., 2019), slowed infant growth (Criswell et al., 2017), and early child behavioural problems (Forns et al., 2016). Thus, the residue levels of POPs in breast milk and their related health consequences on infants are of high concern (Gascon et al., 2012; Mamontova et al., 2017; van den Berg et al., 2017; WHO, 2020).

Previously, the WHO conducted several global surveys on POPs in breast milk sampled from 52 countries (van den Berg et al., 2017), but information about the residue levels of POPs in breast milk in China is limited. Kuang et al. (2020) and Wu et al. (2020) reviewed the residue levels of organochlorine pesticides (OCPs) and PBDEs in breast milk in China and evaluated their associated health risks, respectively. One study summarised the human external exposure pathways of PBDEs and compared the PBDE concentrations in different samples worldwide (Wu et al., 2020). Another study elucidated the spatial distribution, time trends, and health risks of predominant OCPs (Kuang et al., 2020). Several original national studies also reported the body burden of POPs in mothers and evaluated their health risks to breastfed infants (Li et al., 2009; Liu et al., 2010; Zhang et al., 2011; Zhou et al., 2011; Zhang et al., 2016; Shi et al., 2017a; Xia et al., 2016; Xia et al., 2017; Zhang et al., 2017a). Nevertheless, there is still limited comprehensive understanding of the concentrations of traditional and new POPs and their potential health risks.

To address this gap, we conducted a literature review to 1) estimate the average concentrations of individual POPs in breast milk in China, 2) summarise the characteristics of POP exposure levels in breast milk, including the dominant component in each group of POPs, and geographical signature, time trend, and potential exposure sources of certain POPs, and 3) carry out a health risk assessment for breastfed infants.

2. Review methodology and data analysis

2.1. Search strategy and selection criteria

We searched PubMed, Web of Science, and two Chinese databases (CNKI, and Wan-fang databases) for articles related to POP concentrations in breast milk. The search keywords were "persistent organic pollutants" or the abbreviated term "POPs", "polychlorinated biphenyls" or the abbreviated term "PCBs", "organochlorine pesticides" or the abbreviated term "OCPs", "legacy brominated flame retardants" or the abbreviated term "BFRs", "polybrominated diphenyl ethers" or the abbreviated term "PBDEs", "hexabromocyclododecane" or the abbreviated term "HBCD", "tetrabromobisphenol A" or the abbreviated term "TBBPA", "perfluorinated compounds" or the abbreviated term "PFCs", "chlorinated paraffins" or the abbreviated term "CPs", "breast milk" or "human milk", and "China". The publication time period was limited from 2001 to the present.

We included studies that focused on the general population and provided measurement metrics for concentrations (including arithmetic mean, geometric mean, or median concentrations). We excluded articles that reported on occupational exposure subgroups and those that did not involve original results, such as reviews, meta-analyses, meetings, abstracts, letters, and comments. In total, 79 records were included in the present study. Detailed information can be found in Supplementary Tables S1-S6.

2.2. Average POP concentrations

In this study, the average individual pollutant concentrations in breast milk were calculated based on the following formula (Huang et al., 2017):

$$E_{C_{pollutant}} = \frac{\sum (C_i \times n_i)}{\sum n_i} \tag{1}$$

where $E_{C_{pollutant}}$ (ng/g lipid) is the weighted average concentration from multiple studies (data are listed in Tables 1–2). C_i is the mean concentration of individual substance in a study and n_i is the corresponding sample size, with data summarised in Supplementary Tables S1-S6. Considering the heterogeneity among different concentration metrics (arithmetic mean, geometric mean or median), a uniform metric (mean value) was used to estimate reliable average individual POP levels. We used SPSS (version 22.0, IBM, USA) to analyse the correlation among different metrics (Supplementary Fig. S1). In the present study, the total concentration of a class of substances($\sum E_{C_{pollutant}}$) was the sum of concentrations of the included individual congeners ($E_{C_{pollutant}}$). Due to the lack of available concentration metrics, the individual congeners with concentrations less than the detection limit values were not considered.

2.3. Estimated daily intake of breastfed infants under six months of age

The estimated daily intake (EDI) of individual chemicals was calculated based on the following formula (Chan et al., 2007; Zhang et al., 2012a):

$$EDI = E_{C_{pollutant}} \times \frac{V * F}{bw} \tag{2}$$

where F is the percent concentration of fat in milk (%), V is the volume of an infant's daily milk consumption, and bw is the average infant weight. The F, V and bw values inputted in Eq. (2) were 3.5%, 700 mL, and 5 kg, respectively (Chen et al., 2014). Specifically, the total EDI of dioxin-like PCBs (dl-PCBs) was calculated based on the total toxic equivalent (TEQ) concentration. The total TEQ concentration of dl-PCBs ($\sum PCBs - TEQ$) is the sum of sub_{TEQ} concentrations of PCB congeners, and sub_{TEQ} is defined as a substance concentration multiplied by its corresponding toxic equivalence factor (TEF) (van den Berg et al., 2006).

2.4. Health risk assessment for breastfed infants

The non-carcinogenic risk of individual POPs was assessed based on the hazard quotient (HQ). The HQ is defined as the ratio of a substance's EDI to the corresponding threshold reference value (TRV) (Johnson-Restrepo et al., 2007). The TRV (Table 1) was reported as the acceptable daily intake (ADI) by the National Health Commission of the People's Republic of China, oral reference dose (RfD) by the US Environmental Protection Agency (USEPA), minimal risk level (MRL) by the Agency for Toxic Substances and Disease Registry (ATSDR), or tolerable daily intake (TDI) by the European Food Safety Authority (EFSA) and the European Chemicals Bureau (ECB). In the present study, a newly revised TRV based on the end point of non-carcinogenic effect was given a priority for the HQ calculation.

3. Results and discussion

3.1. Contaminants in breast milk

3.1.1. OCPs

Dichlorodiphenyltrichloroethanes (DDTs, including p,p'-DDT, o,p'-DDT, p,p'-DDE, o,p'-DDE, p,p'-DDD, and o,p'-DDD) and hexachlorocyclohexanes (HCHs, including α-HCH, β-HCH, γ-HCH, and δ-HCH) were the dominant OCPs in breast milk (Fig. 1). High levels and proportions of p, p'-DDE and β-HCH were found in breast milk, with average concentrations of 975 ng/g lipid and 620 ng/g lipid, respectively (Table 1). Compared to other countries, p,p'-DDE and β-HCH levels were higher in China (Fig. 2, supplementary Fig. S2, and Table S7). The China Rural Statistical Yearbook confirmed that OCPs accounted for 80% of the total pesticide use before 1982, implying a large amount of historical DDT and HCH use in China (Grung et al., 2015). In general, the average concentrations of p,p'-DDE (the main metabolite of DDT) in breast milk in China show a decreasing trend during 1998–2013 (Fig. 3A), especially in Guangzhou, Shenyang, Shanghai, and Taiwan (Fig. 2). From the equation in Fig. 3A, the average decline rate of p,p'-DDE in breast milk in China was 17.4% (95% CI: 9.3%–24.7%) per year, which was similar to the decline rate of total DDTs reported before (Kuang et al., 2020). And the half-life of p,p'-DDE and DDTs were both ranged from 4 to 8 years in breast milk (Supplementary Table S8). However, DDTs still remain at a high exposure level in some coastal areas. A recent study (Xu et al., 2016) showed that the DDT concentrations reported from Shengsi Island of the East China Sea were significantly higher than the inland levels during the same period (Fig. 2). The total concentration of DDTs in breast milk was up to 1930 ng/g lipid, with p,p'-DDE accounting for 68.3% of the total DDTs. Although the use of DDT has been banned in China since 1983 and is only acceptable in disease vector control, it is still frequently detected in foodstuffs (Cheng et al., 2020; Zhang et al., 2017b). Residents of coastal areas have a high body burden of DDTs due to the high consumption of fish and other seafoods (Grung et al., 2015; Wong et al., 2005). Regarding HCH, the average concentrations of β-HCH (the main metabolite of HCH) in breast milk in China also decreased over time (Fig. 3B), especially in Guangzhou, Shenyang, Shanghai, and Taiwan (Supplementary Fig. S2). From the equation in Fig. 3B, we found that β-HCH in breast milk in China decreased at an average rate of 22.4% (95% CI: 7.9%–34.8%) per year. In addition to the restricted policies of Chinese authority, the fast decline of β-HCH was probably attributed to its short half-life (referred to HCHs) (Supplementary Table S8). Although several studies reported high HCH contamination in the environment and biota (Grung et al., 2015; Wang et al., 2016a), recent biomonitoring studies showed relatively low residue levels of β-HCH in breast milk (Chen and Santos, 2018; Lu et al., 2015a; Shi et al., 2013).

3.1.2. PFCs

Of all analysed POPs in breast milk, the total concentration of PFCs were the lowest. Perfluorooctanoic acid (PFOA) and perfluorooctane

Table 1
Concentration levels of POPs [a] in breast milk.

Chemical	Total sample size	Concentration range (ng/g lipid)	$E_{C_{pollutant}}$ (ng/g lipid)	EDI (ng/kg bw/day)	RfD (ng/kg bw/day)	HQ
HCB	2226	3.6–101.9	35.1	172	170 [k]	1.01
α-HCH	2447	0.133–63.9	4.82	23.6	8000 [l]	0.00295
β-HCH	3346	0.12–2178	620	3038	50,000 [l]	0.0608
γ-HCH	2469	0.0914–60	6.93	33.9	300 [m]	0.113
δ-HCH	1940	0.0945–17	5.83	28.6		
∑HCHs [b]			638	3124	5000 [n]	0.625
p,p'-DDT	3390	0.414–700	95.3	467	500 [o]	0.934
o,p'-DDT	2348	4.1–80	12.2	59.9		
p,p'-DDE	3481	8.07–3370	975	4779		
o,p'-DDE	1626	3.87–115	7.11	34.8		
p,p'-DDD	2712	0.161–135.8	11.7	57.5		
o,p'–DDD	1647	0.4–27	3.60	17.6		
∑DDTs [c]			1105	5415	10,000 [n]	0.542
Aldrin	1562	0.08–2.6	2.17	10.6	100 [n]	0.106
Dieldrin	563	0.170–1.0	0.766	3.75	100 [n]	0.0375
Methoxychlor	265	0.0388–0.87	0.498	2.44		
Endrin	1562	0.12–3.5	2.87	14.1		
Endrin Ketone	123	0.0594–0.112	0.0829	0.406		
Endrin aldehyde	123	0.0618–0.152	0.102	0.500		
∑Endrin [d]			3.05	15.0	200 [n]	0.0750
Cis-nonachlor	125	0.69–1.2	0.787	3.86		
Trans-nonachlor	1600	1.2–12	3.02	14.8		
Oxychlordane	1742	0.49–6.1	2.57	12.6		
Cis-chlordane	325	0.074–0.51	0.307	1.51		
Trans-chlordane	1562	0.0564–1.0	0.500	2.43		
∑Chlordane [e]			3.38	16.6	500 [n]	0.0332
Heptachlor	1538	0.376–1.5	1.39	6.80		
Heptachlor epoxide	599	0.218–4.3	0.847	4.15		
∑Heptachlor [f]			2.24	11.0	100 [n]	0.110
Endosulfan I	325	0.089–1.3	0.795	3.89		
Endosulfan II	325	0.0497–0.6	0.309	1.51		
Endosulfan sulfate	265	0.0713–1.4	0.799	3.92		
∑Endosulfan [g]			1.90	9.32		
Mirex	1297	0.37–2.4	2.31	11.3	200 [n]	0.0565
Toxaphene (Parlar 26)	298	0.17–0.4	0.354	1.73		
Toxaphene (Parlar 50)	298	0.19–0.6	0.517	2.54		
∑Toxaphene [h]			0.871	4.27	250 [n]	0.0171
∑Dicofol [i]	60	–	10.85	53.2	2000 [n]	0.00543
Pentachlorophenol	11	0.32–12.8	2.15	10.54		
∑OCPs			1812	8878		
∑SCCPs	2893	28.6–16,100	1236	6059	100,000 [p]	0.0606
∑MCCPs	2838	9.05–1501	118	578	23,000 [q]	0.0251
∑LCCPs	36	5.23–14.6	10.1	49.4		
∑CPs			1364	6686		
HBCD	3439	0.944–10.1	6.03	29.5	790,000 [r]	0.0000373
TBBPA	3211	0.41–7.58	4.73	23.2		
BDE-15	264	0.2–0.574	0.371	1.82		
BDE-17	221	0.0028–0.35	0.0632	0.310		
BDE-28	4291	0.0286–1.16	0.280	1.37		
BDE-47	4556	0.021–2.99	0.510	2.50	100 [s]	0.0250
BDE-49	171	0.007–0.07	0.0257	0.126		
BDE-66	251	0.008–0.18	0.0626	0.307		
BDE-71	104	0.01–0.07	0.0347	0.170		
BDE-85	147	0.03–0.46	0.185	0.907		
BDE-99	4432	0.024–1.78	0.133	0.652	100 [s]	0.00652
BDE-100	4451	0.02–1.21	0.104	0.510		
BDE-118	148	0.0363–0.0593	0.0478	0.234		
BDE-119	111	0.011–0.0267	0.0215	0.105		
BDE-138	187	0.001–0.59	0.109	0.533		
BDE-153	4496	0.14–3.66	0.585	2.87	200 [s]	0.0143
BDE-154	4153	0.01–1.39	0.0608	0.298		
BDE-183	4233	0.022–5.81	0.331	1.62		
BDE-184	127	0.02–0.05	0.0301	0.148		
BDE-190	120	0.0231–0.17	0.0494	0.242		
BDE-191	67	0.003–0.03	0.0151	0.0739		
BDE-196	219	0.044–0.46	0.155	0.757		
BDE-197	219	0.07–1.46	0.579	2.84		
BDE-206	159	0.04–0.3	0.156	0.765		
BDE-207	219	0.06–1.13	0.461	2.26		
BDE-209	2318	0.06–9.85	1.43	6.99	7000 [s]	0.00100
∑BFRs			16.6	81.1		
PFOA	1242	0.018–0.814 [j]	0.116 [j]	16.2	1500 [t]	0.0108
PFOS	1382	0.006–0.137 [j]	0.0568 [j]	7.96	150 [t]	0.0531

Table 1 (*continued*)

Chemical	Total sample size	Concentration range (ng/g lipid)	$EC_{pollutant}$ (ng/g lipid)	EDI (ng/kg bw/day)	RfD (ng/kg bw/day)	HQ
PFUdA	1117	0.008–0.196 [j]	0.0373 [j]	5.22		
PFDA	1137	0.003–0.063 [j]	0.0106 [j]	1.49		
PFNA	1317	0.006–0.076 [j]	0.0168 [j]	2.36		
PFHxS	1012	0.003–0.015 [j]	0.00636 [j]	0.891		
∑PFCs			0.244 [j]	34.1		

Abbreviation: PFUdA, Perfluoroundecanoic acid; PFDA, Perfluorodecanoic acid; PFNA, Perfluorononanoic acid; PFHxS, Perfluorohexane sulfonate.
[a] PCBs is separately listed in Table 2.
[b] Sum of α-HCH, β-HCH, δ-HCH, and γ-HCH.
[c] Sum of p,p'-DDT, o,p'-DDT, p,p'-DDE, o,p'-DDE, p,p' –DDD, and o,p'–DDD.
[d] Sum of Endrin, Endrin Ketone, and Endrin aldehyde.
[e] Sum of Cis-chlordane, Trans-chlordane, and Oxychlordane.
[f] Sum of Heptachlor and Heptachlor epoxide.
[g] Sum of Endosulfan I, Endosulfan II, and Endosulfan sulfate.
[h] Sum of Toxaphene (Parlar 26) and Toxaphene (Parlar 50).
[i] Sum of o,p'-Dicofol and p,p'- Dicofol.
[j] The levels of PFCs are expressed on wet weight (ng/mL).
[k] Cited from (EFSA, 2006).
[l] Cited from (ATSDR, 2005).
[m] Cited from (USEPA, 1987).
[n] Cited from GB 2763–2019 (National Health Commission of the People's Republic of China, 2019).
[o] Cited from (USEPA, 1987).
[p] Cited from (ECB, 2007).
[q] Cited from (ECB, 2008).
[r] Cited from (EFSA, 2011a).
[s] Cited from (EFSA, 2011b).
[t] Cited from (EFSA, 2008).

sulfonic acid (PFOS) were two dominant pollutants, with concentrations of 0.116 ng/mL and 0.0568 ng/mL, respectively (Table 1). Liu et al. (2011) analysed PFCs in matched maternal serum and breast milk and reported that the median partition ratio between human milk and maternal serum was from 0.02:1 (PFOS) to 0.09:1 (PFOA) for five detectable PFCs. The lower PFC concentrations in breast milk are attributed to the strong binding capacity of PFCs with proteins in maternal blood, which limits the possibility of PFCs entering breast milk (Liu et al., 2010). Nevertheless, postnatal exposure to PFCs through breastfeeding has been verified in humans (Karrman et al., 2007; Tao et al., 2008a). The current levels of PFOA and PFOS in breast milk are comparable around the world (Supplementary Table S9). However, a national survey of 12 representative areas in mainland China showed that significantly high levels of PFCs in breast milk were sampled from Shanghai. The concentration of PFOA was even higher than that reported in some developed countries (USA, Italy, Spain, Japan, and Korea) (Barbarossa et al., 2013; Fujii et al., 2012; Motas Guzmàn et al., 2016; Tao et al., 2008b). The high level of PFOA in Shanghai is probably related to the industrial discharge of PFOA from a number of fluoropolymer manufacturing facilities (Song et al., 2018; Wang et al., 2016b). In addition, contaminated water sources increased PFOA exposure in residents of Shanghai (So et al., 2007). There is increasing concern about the importance of dietary PFC exposure in the general population (Fromme et al., 2009; Jian et al., 2017; Wang et al., 2015).

Table 2
Concentration levels of PCBs in breast milk.

Chemical	Total sample size	Concentration range (ng/g lipid)	$EC_{pollutant}$ (ng/g lipid)	EDI (ng /kg bw/day)	RfD (ng/kg bw/day)	HQ	TEF (2005)	Sub_{TEQ} (pg TEQ/g lipid)	EDI (pg TEQ/kg bw/day)
PCB 28	3199	0.73–3.07	1.23	6.03					
PCB 52	3199	0.04–0.389	0.138	0.674					
PCB 101	3199	0.06–0.99	0.151	0.741					
PCB 138	3199	2.22–17.7	3.28	16.1					
PCB 153	3251	1.83–21.2	3.88	19.0					
PCB 180	3199	0.65–14.1	0.952	4.66					
∑non-dioxin-like PCBs			9.63	47.2	10 [a]	4.72			
PCB 105	3029	0.0717–2.43	0.685				0.0003	0.206	1.01
PCB 114	3029	0.0257–0.276	0.123				0.0003	0.0369	0.181
PCB 118	3054	0.395–6.4	2.18				0.0003	0.653	3.20
PCB 123	3029	0.0039–0.202	0.0360				0.0003	0.0108	0.0528
PCB 156	3029	0.0846–1.88	0.669				0.0003	0.201	0.983
PCB 157	3029	0.0209–0.398	0.151				0.0003	0.0452	0.222
PCB 167	3029	0.0228–0.73	0.211				0.0003	0.0632	0.310
PCB 189	3029	0.0057–0.14	0.0479				0.0003	0.0144	0.0704
∑Mono-ortho PCB-TEQ			4.10					1.23	6.03
PCB 77	3029	0.0009–0.0152	0.00517				0.0001	0.000517	0.00254
PCB 81	3029	0.0004–0.0063	0.00270				0.0003	0.000810	0.00397
PCB 126	3029	0.0023–0.0327	0.0156				0.1	1.56	7.64
PCB 169	2919	0.0008–0.0302	0.0115				0.03	0.344	1.69
∑Non-ortho PCB-TEQ			0.0350					1.91	**9.34**
∑dl-PCBs			4.14					3.14	15.4

[a] Cited from (EFSA, 2005).

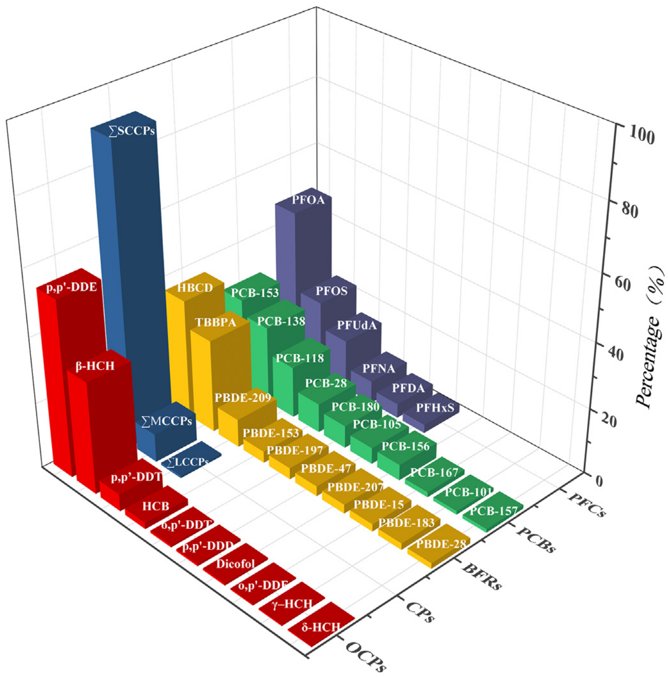

Fig. 1. Congener contribution (%) of each group of POPs in breast milk, in which the top ten single substances of OCPs, PBDEs and PCBs were listed.

The findings suggested that fish and shellfish consumption exhibited the highest PFC exposure among all foodstuffs, followed by eggs and meat products, and vegetables were the lowest. Thus, we should further focus on the PFC exposure from dietary intake.

3.1.3. CPs

Short-chain chlorinated paraffins (SCCPs) were the highest in breast milk (Fig. 1), with a concentration of 1236 ng/g lipid (Table 1). Compared to median-chain chlorinated paraffins (MCCPs) and long-chain chlorinated paraffin (LCCPs), SCCPs have shown the highest toxic potential, and they markedly increase in contamination in the environment and biota, and therefore have attracted particular attention (Zeng et al., 2015; van Mourik et al., 2016). However, as alternatives to SCCPs, the use of MCCPs and LCCPs is gradually increasing, but information regarding their conclusive risk assessment is limited or entirely lacking. A recent review conducted an investigation of the global CP production volume and showed that 15% of the total global CP production in 2013 was from China, reaching 1.05 million tons (van Mourik et al., 2016). This report demonstrated high CP exposure levels in China. The average concentrations of CP congeners in breast milk in China were indeed higher than that reported in Sweden and Norway (Zhou and Yuan, 2020), the UK (Thomas et al., 2006), and Japan and Korea (Cao et al., 2017) (Supplementary Fig. S3). Regarding the biomonitoring studies in China, two national studies (Xia et al., 2016; Xia et al., 2017) suggested that women living in urban areas have higher CP exposure levels than women living in rural areas. Henan and Hebei urban regions presented the highest levels of CPs because these two provinces are the major Chinese CP production sites and characterised by high

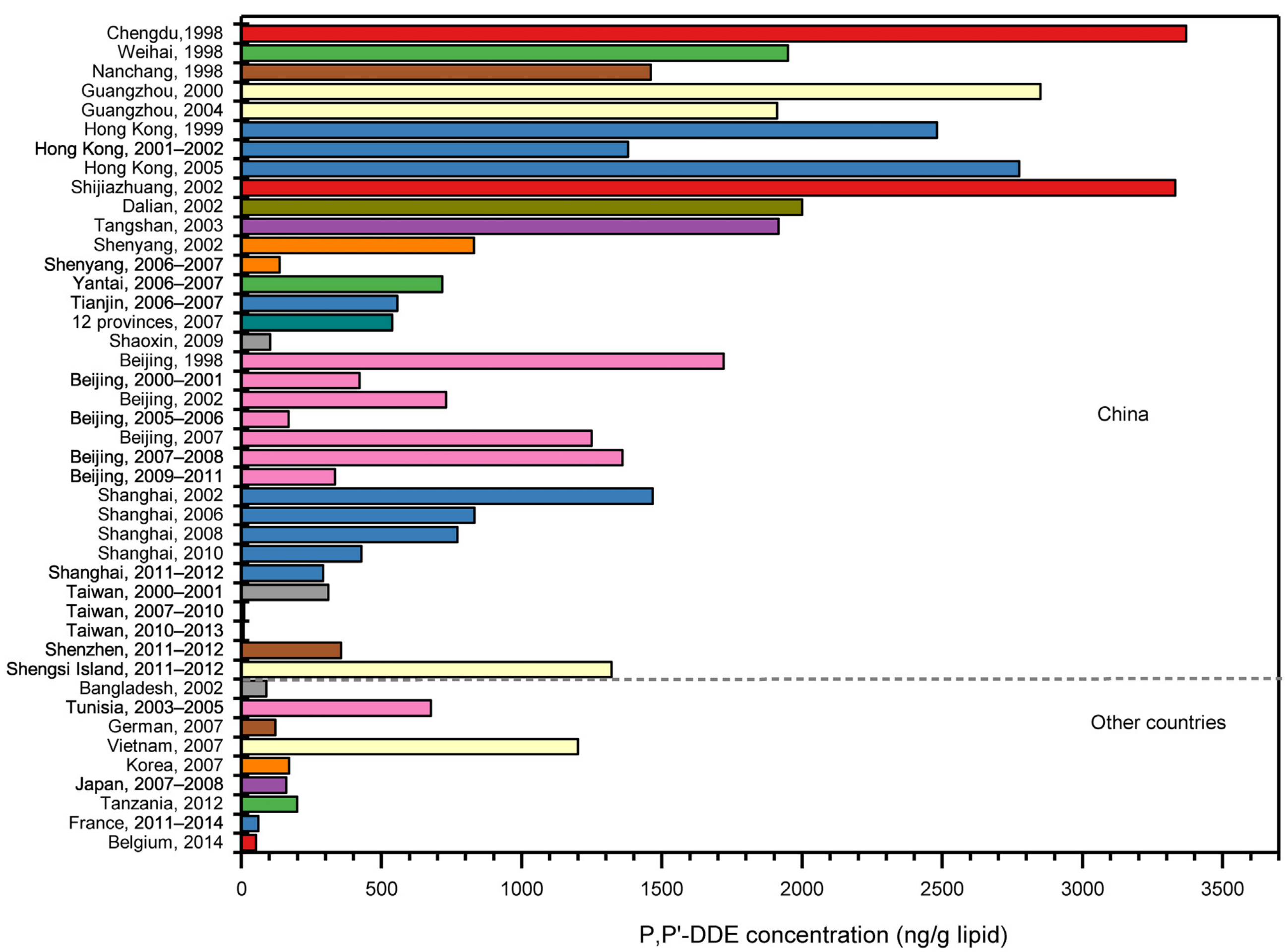

Fig. 2. Levels of p,p'-DDE in breast milk among various regions.

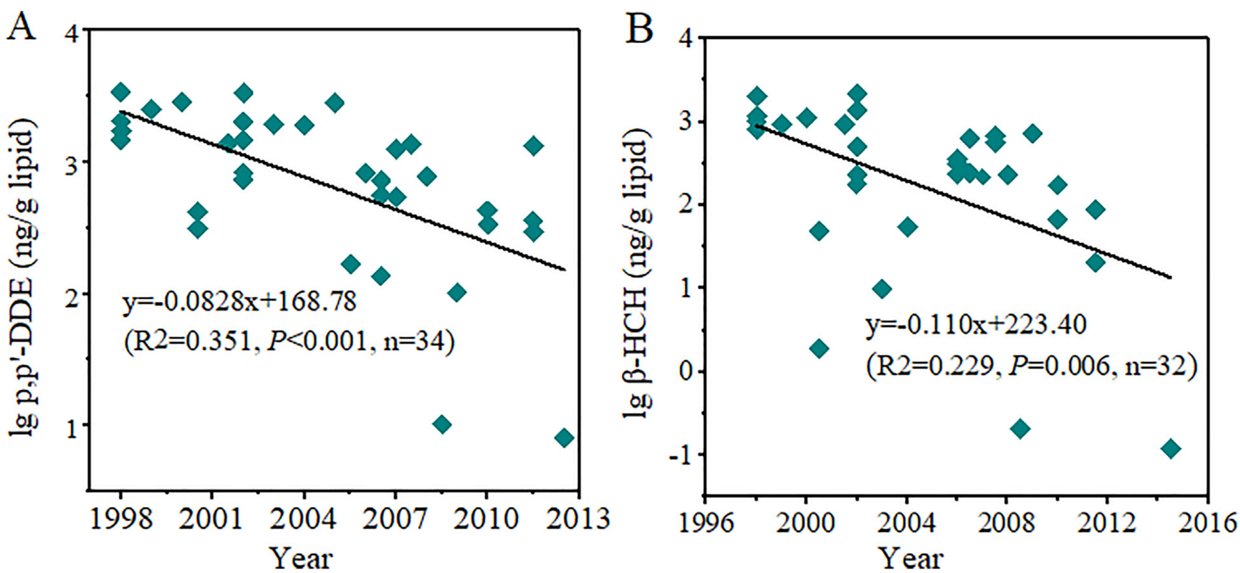

Fig. 3. Relationships between p,p'-DDE (A) and β-HCH (B) residues in breast milk and the year. Note: The concentrations of p,p'-DDE and β-HCH in Table S1 were included. Moreover, when the sampling time lasted for several years, the average year were used.

industrialisation (Xia et al., 2016). A recent study reported a high concentration of CPs in breast milk sampled from Mianyang (Liu et al., 2020), which is an industrial city in Sichuan province, China. CP contamination in this district was mainly attributed to the production and use of substantial amounts of industrial products (for example, metal wear-resistant products and insulation materials), and therefore local residents have a high body burden of CPs. The Pearl River Delta has been given special focus due to its high urbanisation and industrialisation (Wang et al., 2013; Zeng et al., 2017). In the Pearl River Delta, CPs are ubiquitous in the environment and are frequently detected in most natural environmental media (Chen et al., 2011; Wang et al., 2013; Zeng et al., 2017), as well as indoor environments (Zhuo et al., 2019). The CP exposure levels in the indoor environment were even higher than in the outdoor environment (Zhuo et al., 2019). Humans spend most of the time in indoors, especially infants and toddlers. Thus, we speculated that Pearl River Delta residents probably have a high body burden of CPs. However, investigations of human CP exposure levels and associated health risks are scarce in the south coast of China.

3.1.4. BFRs

The BFR concentrations were relatively low in breast milk, among which the three main BFRs are decabrominated diphenyl ether (BDE-209), hexabromocyclododecane (HBCD), and tetrabromobisphenol A (TBBPA). At present, PBDE and HBCD are listed as POPs, whereas TBBPA is not (UNEP, 2017). The calculated average level of BDE-209 was 1.43 ng/g lipid in the present study, which was slightly higher than that reported from a national survey (Shi et al., 2017a), and lower than that in a recent study in Beijing (Chen et al., 2019). The study in Beijing suggested that levels of tri- to hepta-BDEs significantly declined from 2005 to 2014, whereas BDE-209 showed no significant variation from 2011 to 2014. Compared to other countries, the levels of PBDEs in breast milk in China were in low or moderate (Chen et al., 2019). PBDEs have been produced as three commercial mixture: penta-, octa-, and deca-BDEs. The former two products were phased out globally after they were listed as POPs in 2009 (UNEP, 2009). Deca-BDE was also listed as POPs by Stockholm Convention in 2017 (UNEP, 2017). In China, octa-BDE and penta-BDE were banned in 2004, whereas there is no regulatory action on deca-BDE (Ni et al., 2013; Shi et al., 2018). Jin et al. (2009) monitored PBDE levels in the breast milk of residents living near the deca-BDE production area of Laizhou Bay and found that BDE-209 was an abundant congener; thus, the extensive industrial usage of deca-BDE could be a source for people with a high body burden of BDE-209. The estimated average level of HBCD in the present study was higher than that of BDE-209, with a concentration of 6.03 ng/g lipid. The average HBCD in China was significantly higher than in studies in India (Devanathan et al., 2012), Vietnam (Tue et al., 2010), Russia (Polder et al., 2008), Norway (Thomsen et al., 2010), Belgium (Croes et al., 2012), and Canada (Ryan and Rawn, 2014), comparable to studies in Australia (Toms et al., 2012) and the UK (Abdallah and Harrad, 2011), and lower than a study in Spain (Eljarrat et al., 2009). The high HBCD concentration in our study is attributed to the contribution of the residue level reported in a recent national study (Shi et al., 2017a). A recent study conducted in Shenzhen showed that HBCD level (1.82 ng/g lipid) in China was comparable to other countries. Three HBCD diastereoisomers could be detected in breast milk, among which α-HBCD was usually predominant (Lu et al., 2018). The different concentration distributions of the diastereoisomers in organisms were attributed to their selective metabolism and biotransformation (Zegers et al., 2005; Erratico et al., 2016). According to the report from the fifth Chinese total dietary study (Shi et al., 2017b), we found that meat and meat products were the main source of BFR intake in non-occupational populations because the consumption of meat and meat products in the Chinese population was significantly higher than that of other fatty food groups. In addition, the usage of HBCD in building materials is still permitted, which increases the body burden of HBCD among the Chinese population (Shi et al., 2018). The average concentration of TBBPA in breast milk was 4.73 ng/g lipid in this study. Uncertainty persists due to the limited investigations of TBBPA in breast milk in China and the large variations in data among the present studies. The report from the fourth Chinese total dietary study (TDS) and Nation Human Milk Survey (NHMS) showed a sharp increase in the average TBBPA level in foodstuffs and breast milk from 2007 to 2011 (Shi et al., 2009; Shi et al., 2017b), which is related to the restriction of PBDEs and the high degree of alternative TBBPA usage. Although reported studies to date have shown no health risks for those exposed to TBBPA, additional research should be conducted to fully understand the human body burden of TBBPA.

3.1.5. PCBs

PCBs are grouped into non-dioxin-like PCBs and dl-PCBs. To evaluate the toxicity of dl-PCBs to polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs), the sub_{TEQ} concentrations of PCB congeners and the total TEQ concentration of dl-PCBs ($\sum$PCBs − TEQ) were calculated (Table 2). In the present study, the average $\sum$PCBs − TEQ (3.14 pg TEQ/g lipid) was higher than the results from a national study in mainland China (Zhang et al., 2011), Beijing (Bao et al., 2020), Shanghai (Lu et al., 2015b), Shijiazhuang (Sun et al., 2011), and Zhejiang (Shen et al., 2012), comparable to that reported in Hong Kong in 2009 (Wong et al., 2013), and lower than that assessed in Hong Kong in 2002 (Hedley et al., 2006), and Shenzhen (Deng et al., 2012). The national study showed that the highest TEQ body burden for women from Shanghai was positively related to a higher level of industrialisation and a higher fatty food intake. A recent study (Lu et al., 2015b) conducted in Shanghai from 2011 to 2012 suggested that the TEQ in human milks is related to rapid urbanisation and industrialisation. In addition, mothers who consumed both fresh water and marine fish had a higher body burden of dl-PCBs than those who consumed freshwater fish only. Compared to an earlier Hong Kong study in 2002 (Hedley et al., 2006), the average $\sum$PCBs − TEQ level in the latest finding was approximately 19% lower (Wong et al., 2013), indicating the positive effect of some policies on reducing and eliminating PCBs. Compared to other countries, the total TEQ concentration of dl-PCBs in China was indeed lower than in developed countries (Canada, France, Sweden, and Slovakia) (Antignac et al., 2016; Chovancova et al., 2011; Fang et al., 2013; Rawn et al., 2017). To identify the contribution of single PCB congeners to the total TEQ, the contribution of the sub_{TEQ} values of 12 PCB congeners to $\sum$PCBs − TEQ is displayed in Supplementary Fig. S4. The highest contribution of 12 PCB congeners was attributed to $sub_{TEQ-PCB126}$, which was consistent with many previous results (Deng et al., 2012; Li et al., 2009; Wittsiepe et al., 2007). For non-dioxin-like PCBs, our study included 6 indicator PCBs (Nos. 28, 52, 101, 138, 153, and 180). The variations in their concentrations in breast milk were minor, almost all of which were within one magnitude. The total concentration of the six indicator PCBs in this study (Σ_6PCBs=9.63 ng/g lipid) was higher than the result in Beijing (Bao et al., 2016) and the concentration (Σ_6PCBs=6.6 ng/g lipid) determined in a recent national study (Zhang et al., 2017a), and lower than the levels reported in Zhejiang (Shen et al., 2012) and Shenzhen (Deng et al., 2012). Women in Shenzhen have a higher body burden of total PCBs compared to the other non-exposed regions in mainland China, which is attributed to a dense population and developed industry in this district (Tang et al., 2020). Shenzhen is located at the east of the Pearl River Delta, which is one of the most economically developed coastal cities in China. Rapid economic growth has had a significant impact on the environmental PCB levels (Duan et al., 2013). Large amounts of domestic sewage and industrial wastewater were found to be discharged into Shenzhen's coastal areas and most likely to be the source of high PCB concentrations in surface sediments in this region (Tang et al., 2020). Compared to data from the latest global breast milk biomonitoring report during 2008–2012 (UNEP, 2013), the concentration of indicator PCBs in this present study was similar to the levels monitored from some countries or regions with low industrialisation, indicating relatively low residue levels of PCBs in breast milk in China. By comparing the concentrations of indicator PCBs with those of dl-PCB in breast milk, the indicator PCBs were distinctly regarded as the main pollutants, with an average concentration of 9.63 ng/g lipid (Table 2).

3.2. EDI and health risk assessment

Breastfeeding is essential for infant growth and development, as well as for infection prevention and cognitive improvement. However, epidemiological studies have showed that the potential health risks for infants exposed to POPs through breastfeeding have been recognised (Lehmann et al., 2014; Wohlfahrt-Veje et al., 2014; Lignell et al., 2016; Lenters et al., 2019), while few studies have conducted a comprehensive health risk assessment on these chemicals. The non-carcinogenic risk of individual pollutants was assessed using the HQ, which was calculated by dividing the EDI by the corresponding TRV. If HQ > 1, infants are likely to suffer adverse health effects from exposure to POPs. If HQ < 1, it is an

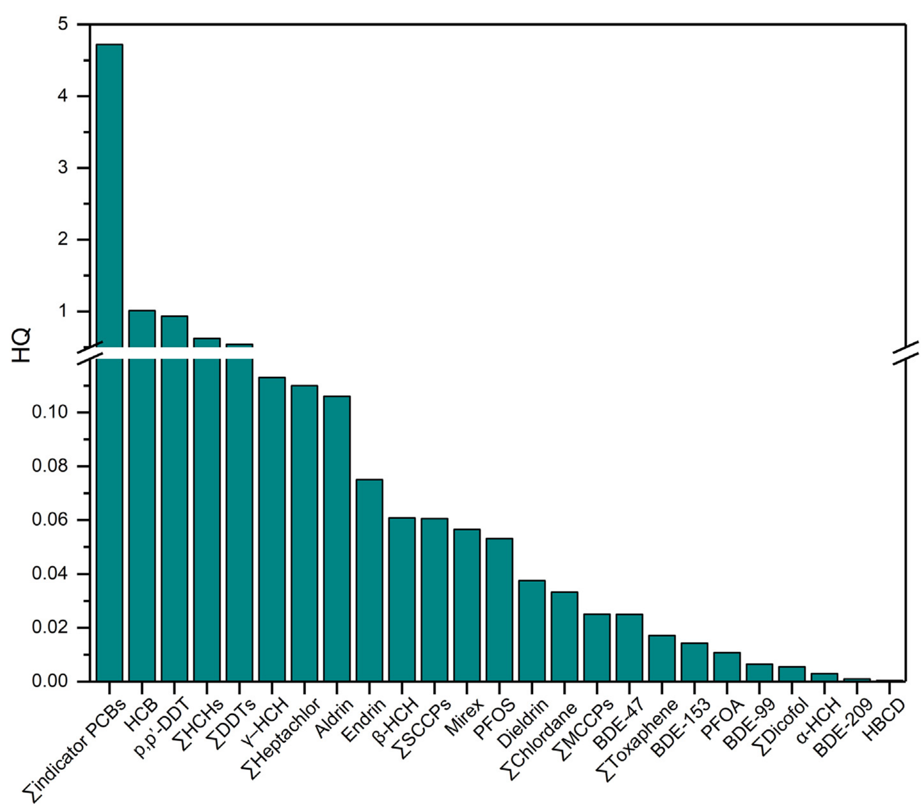

Fig. 4. The order rank of HQ of POPs (except for dl-PCBs).

acceptable level (Devanathan et al., 2012). In addition to the HQ method, the margin of exposure (MOE) approach is also suitable for assessing the potential health risks of specific contaminants from dietary intake, especially for BFRs and CPs (Wang et al., 2019; Zhou and Yuan, 2020). Considering the consistency and feasibility for risk assessment on all of the included POPs, we uniformly applied the HQ approach to evaluate the potential health risks for breastfed infants in the present study. The risk assessment for BFRs and CPs using MOE approach is provided in the supplementary materials (Tables S10-S11).

According to the HQ and MOE values, breastfed infants in China probably suffered potential health risks from exposure to DDT, hexachlorobenzene (HCB), and PCBs (Fig. 4, and Tables S10-S11). Thus, we further discussed the health risks of DDT, HCB, and PCBs in detail.

Regarding p,p'-DDT, the average EDI of p,p'-DDT (467 ng/kg bw/day) in our study was higher than that in studies in Belgium (Aerts et al., 2019), eastern Siberia, Russia (Mamontova et al., 2017), Bangladesh (Haque et al., 2017), and northern Tanzania (Muller et al., 2017), comparable to that in an Indian study (Bedi et al., 2013), and lower than that in southwestern Ethiopia (Gebremichael et al., 2013) and Tunisia (Hassine et al., 2012), demonstrating higher DDT contamination in some Asian and African countries. To recognise the geographical signature and time trend of EDIs of p,p'-DDT, we produced a histogram of EDIs of p,p'-DDT in different areas in China (Fig. 5) and found that the maximum EDI for breastfed infants (3430 ng/kg bw/day) was in a study conducted in Guangzhou (Wong et al., 2002), followed by Shengsi Island (Xu et al., 2016) and other areas. The high level of p,p'-DDT in breast milk sampled from Guangzhou was related to high contamination in environmental media and aquatic organisms (Hong et al., 1999). Guangzhou is a well-developed coastal city and generates a large quantity of waste in the process of urban and industrial development, so POPs are a major environmental issue (Wong et al., 2002). Surprisingly, Shengsi Island located adjacent to Shanghai, had a significantly higher p,p'-DDT concentration in breast milk sampled between 2011 and 2012 than Shanghai (Lu et al., 2015a; Xu et al., 2016). The higher p,p'-DDT concentration in Shengsi Island was associated with its location and residents' dietary sources. Shengsi Island is located at the Yangtze River outlet and central to the largest fishing ground (Zhoushan Island) in China. The unique location makes it more susceptible to pollution discharged into the Yangtze River. Elevated DDT levels in the environmental media resulted in relatively high background levels in Shengsi Island (Li et al., 2008). Moreover, Shengsi Island's residents are fish consumers, and high DDT contamination was found in meat, seafoods, and dairy products (Zhang et al., 2012b; Zhou et al., 2014). Thus, mothers living on the island have a higher body burden of DDT and their infants suffered a higher risk of DDT exposure through breastfeeding. In fact, the EDIs of p,p'-DDT were significantly decreased over time in Guangzhou, Beijing, Shanghai, and Taiwan (Fig. 5). In addition to Shengsi Island (Xu et al., 2016), the EDI of p,p'-DDT in infants in China was within the acceptable levels after 2006 (Haraguchi et al., 2009; Leng et al., 2009; Lu et al., 2015a; Song et al., 2013; Tao et al., 2008c; Zhou et al., 2011; Zhou et al., 2012a; Zhou et al., 2012b). The average daily intake of p,p'-DDT in breastfed infants on Shengsi Island was 2.33 μg/kg bw/day, which exceeded an oral reference dose suggested by the USEPA (0.5 μg/kg bw/day) (USEPA, 1987), implying the potential health risk from DDT exposure in China's east coastal regions. The health effects of DDT exposure have been extensively studied, and adverse health effects in the neonatal or early childhood period have been implicated (Chevrier et al., 2019; Coker et al., 2018; Xu et al.,

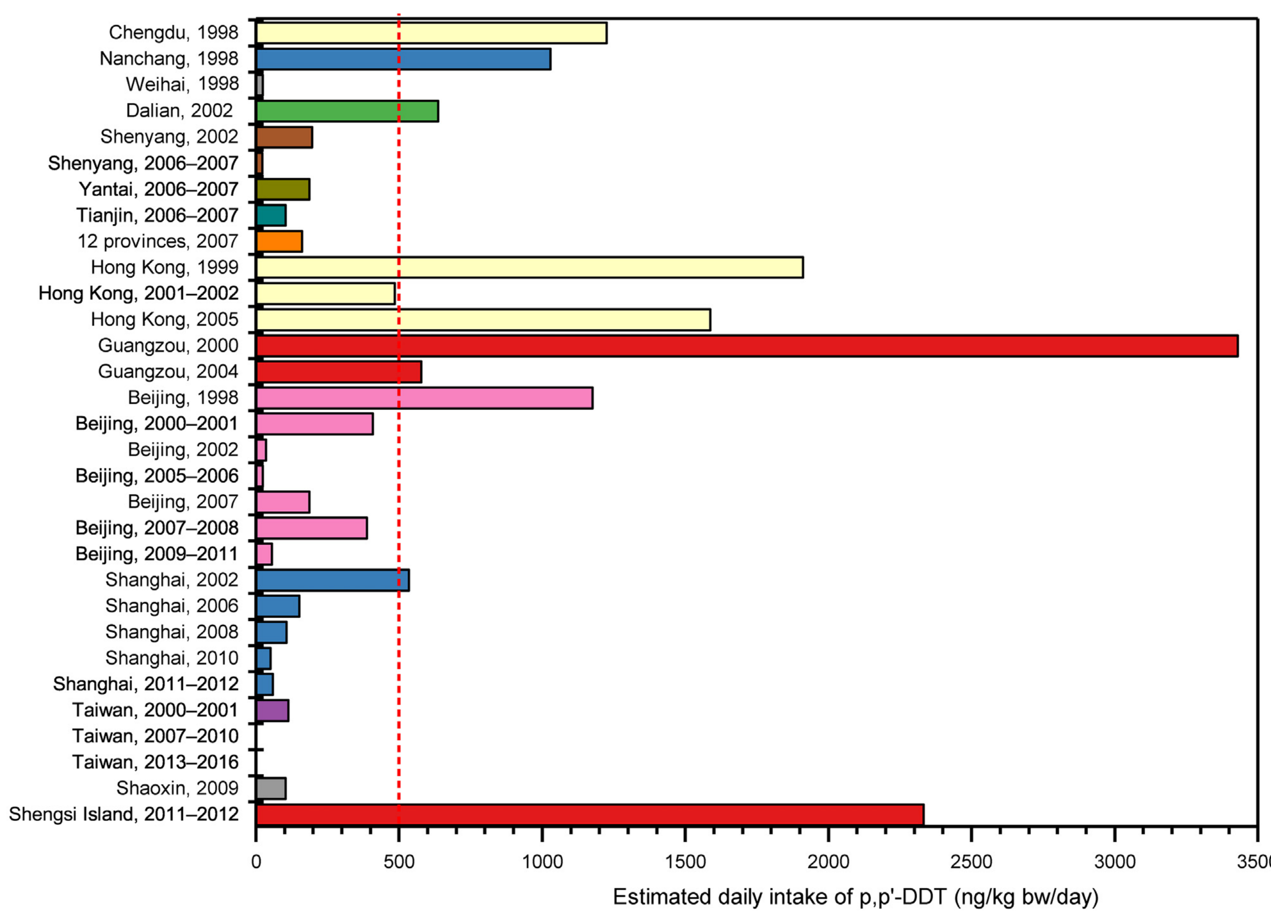

Fig. 5. Estimated daily intakes of p, p'-DDT through breastfeeding among various regions (red dotted-line represents the threshold reference value of p, p'-DDT for breastfed infants). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

2017). Effects on thyroid hormones or the anthropometric development of foetuses have been reported (Al-Saleh et al., 2012; Arrebola et al., 2016; Asawasinsopon et al., 2006; Bravo et al., 2019; Chevrier et al., 2019), and these results are consistent. Greater attention has been paid to the health effects of DDT and/or DDE on neurotoxicity (Burns et al., 2013; Eriksson, 1997; Johansson et al., 2008; Mariussen and Fonnum, 2006). Damage to neurocognitive and behavioural development has been observed in breastfed infants (Kao et al., 2019; Saeedi Saravi and Dehpour, 2016).

HCB was first introduced as an agricultural pesticide in 1945. It was also a by-product of industrial chemical manufacturing process and is presented as an impurity in several pesticide formulations (UNEP, 2001). The average EDI of HCB (172 ng/kg bw/day) in our study was higher than in studies in Japan (Kunisue et al., 2006), India (Subramanian et al., 2007), European countries (Aerts et al., 2019; Antignac et al., 2016), and the US (Johnson-Restrepo et al., 2007), comparable to a Russian study (Tsydenova et al., 2007), and lower than in Tunisia (Hassine et al., 2012). Compared to reported global levels, the residue level of HCB in breast milk in China is markedly high. The EDI of HCB in infants born in most nationwide areas exceeds the TDI (170 ng/kg bw/day) recommended by the EFSA (EFSA, 2006), suggesting a potential health risk in infants exposed to HCB through breastfeeding (Fig. 6). As depicted in Fig. 6, no special geographical HCB signature was observed. Nevertheless, women living in the northern China including Shijiazhuang, Tangshan, Beijing, and Dalian have a slightly higher body burden of HCB than those in southern China (Supplementary Table S1), which is probably related to the seriously contaminated food and polluted air in these regions. Fu et al. (2018) found higher HCB residue levels in freshwater products sampled from northeast China than from the southern city of Guangzhou. A recent study (Yu et al., 2019) confirmed that ambient air in littoral cities in northern China contained a higher HCB level than Ningbo in southern China. There is no significant downward trend of HCB in breast milk in China (Supplementary Fig. S5). This finding is probably attributed to the recent input of HCB, as HCB's production and use was not completely banned until 2009 in China (Die et al., 2014). Besides, there are some potential unintended HCB emission sources (Wang et al., 2010a). Continuous monitoring of HCB in breast milk is needed, since a high concentration of HCB in mothers is related to slower infant growth (Stigum et al., 2015), decreased foetal thyroid hormones (Li et al., 2014), and reduced cognitive development in early childhood (Kyriklaki et al., 2016).

Regarding indicator PCBs, six congeners were estimated in the present study, and the total EDI was 47.2 ng/kg bw/day (Table 2). PCB 153 and PCB 138 were two predominant components and accounted for 40.3% and 34.1% of the total daily intake of indicator PCBs, respectively (Supplementary Fig. S6), followed by PCB 28 > PCB 180 > PCB 101 > PCB 52. The PCB congener profiles are basically similar among eight included studies (Fig. 7). However, the PCB congener profiles of human milk in China differ from those in other countries (Wang et al., 2010b). The proportion of tri-PCB (PCB-28) is higher in China than in European countries, whereas the percentage of hepta-PCB (PCB-180) is higher in European countries. Due to the lack of available literature on health-based guidance values for non-dioxin-like PCBs, the health risks of breastfed infants regarding non-dioxin-like PCBs are not commonly assessed. The Second PCB Workshop in Brno (May 2002) set a

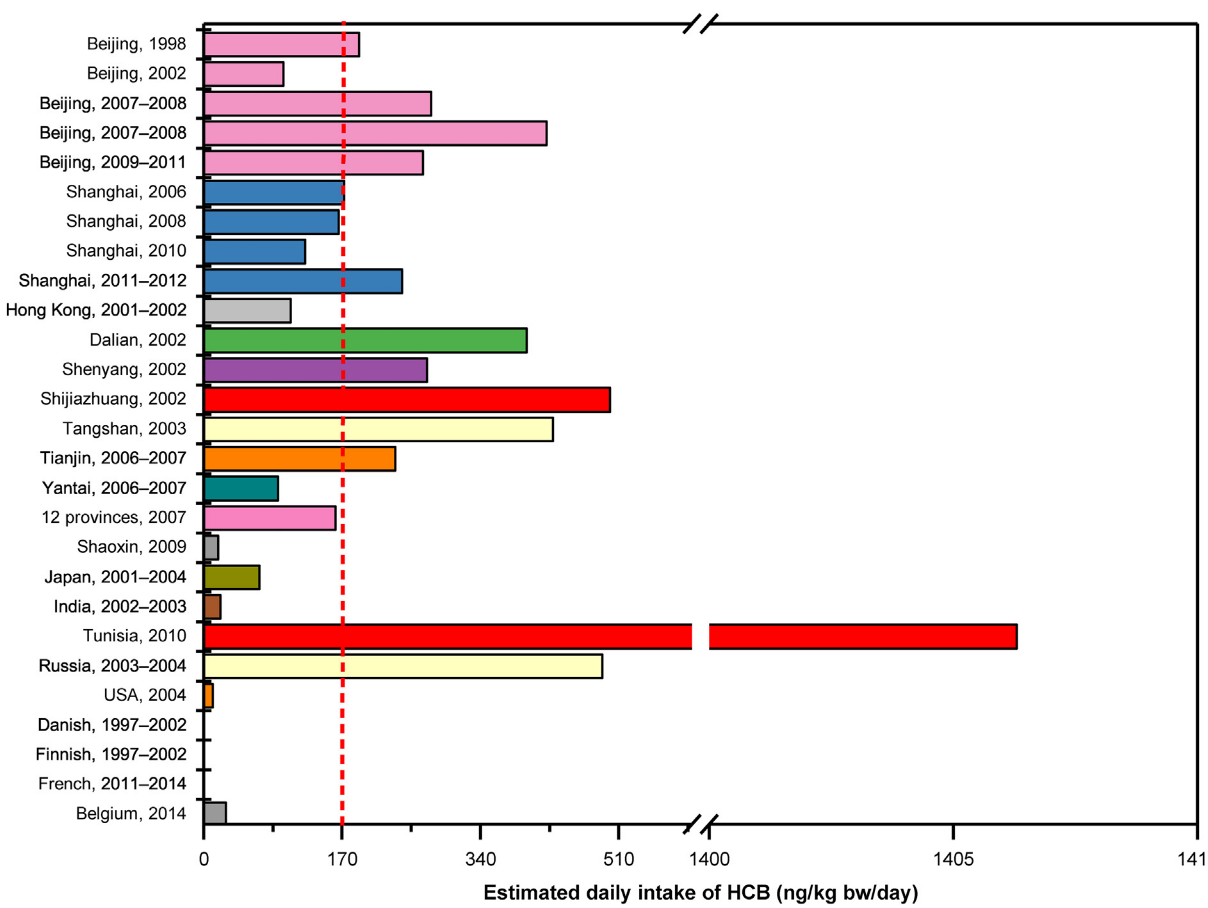

Fig. 6. Estimated daily intakes of HCB through breastfeeding among various regions (red dotted-line represents the threshold reference value of HCB for breastfed infants). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

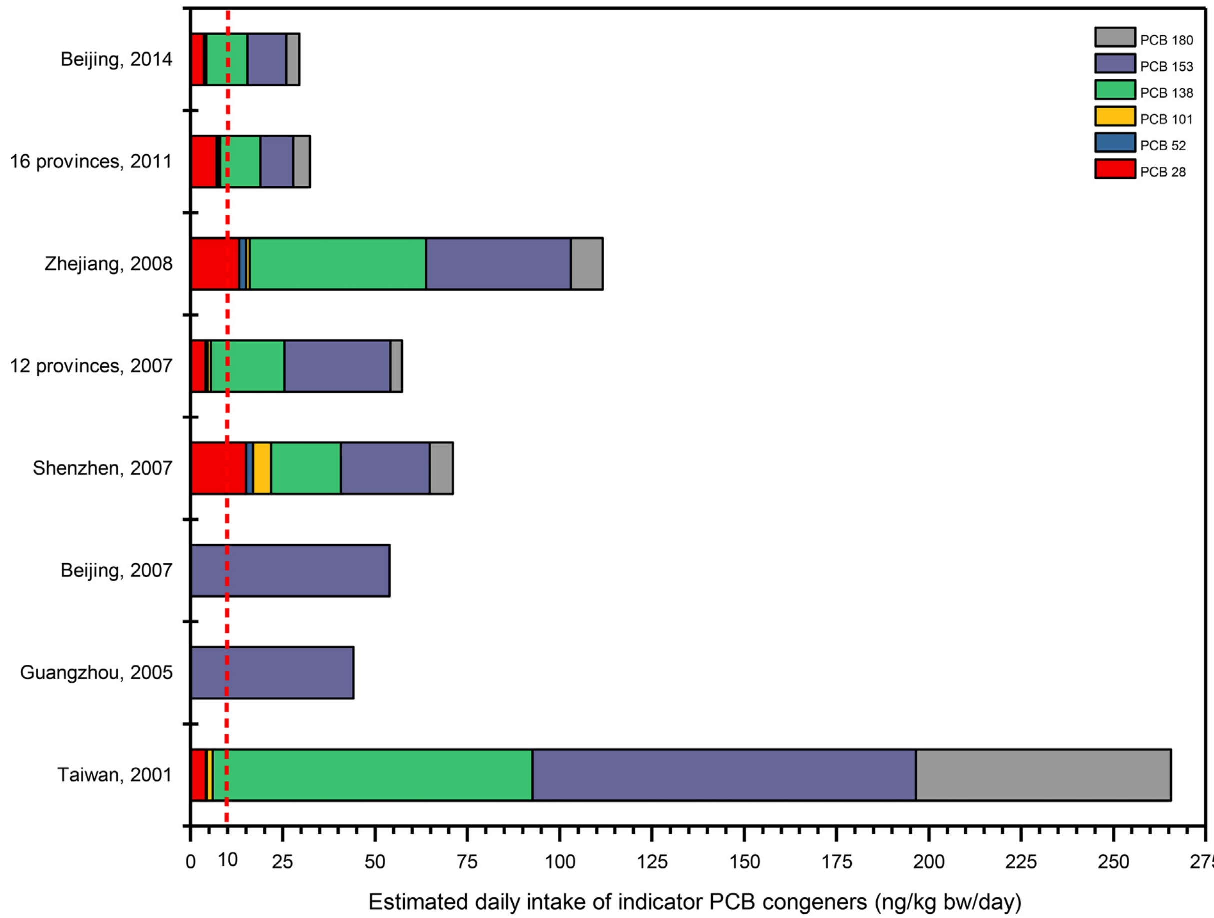

Fig. 7. Estimated daily intakes of indicator PCB congeners through breastfeeding among different regions (red dotted-line represents the threshold reference value of total indicator PCBs for breastfed infants). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

provisional tolerable intake (PTDI) of 20 ng/kg bw/day for all 209 PCBs (AFSSA, 2007). A PTDI for indicator PCBs of 10 ng/kg bw/day was proposed since half of the total daily intake of PCBs consisted of six indicator PCBs (EFSA, 2005). The average EDI of indicator PCBs in the present study exceeds the PTDI value, thus gaining an HQ value of 4.72 (Fig. 4 and Table 2). This result suggested that some measures should be made to eliminate PCB contamination. For the whole country, the average concentrations of indicator PCBs decreased in breast milk during 2001–2014 (Supplementary Fig. S7A). The annual decline rate of indicator PCBs in breast milk in China was 13.9% (95% CI: 3.7%–22.9%). Nevertheless, the average EDIs of total indicator PCBs in the eight studies (Bao et al., 2016; Bi et al., 2006; Chao et al., 2003; Deng et al., 2012; Haraguchi et al., 2009; Shen et al., 2012; Zhang et al., 2011; Zhang et al., 2017a) were significantly higher than the PTDI value (Fig. 7). Biomonitoring survey still need to be conducted at a nationwide scale to monitor the levels of indicator PCBs. The body burden of dl-PCBs is expressed in picograms of dioxin total toxic equivalent per gram of fat in breast milk. The EDI of dl-PCBs for breastfed infants is therefore expressed as pg TEQ/kg bw/day. By comparison with an oral reference dose proposed by the USEPA (RfD of 0.7 pg TEQ/kg bw/day for dl-PCBs) or a recently revised tolerable weekly intake (TWI of 2 pg TEQ/kg bw/day for dioxin and dl-PCBs) (USEPA, 2010; EFSA, 2018), the sum of EDI value of dl-PCBs in the present study (15.4 pg TEQ/kg bw/day) was obviously above the safety standard, indicating that some source-directed measures should be taken to reduce human exposure to dl-PCBs. Two recent studies conducted in Beijing (Bao et al., 2020) and Guangdong province (Huang et al., 2019) showed that the mean TEQ concentration (calculated with TEFWHO 2005) of dl-PCBs (2.0 pg/g lipid in 2013–2015 vs 2.24 pg/g lipid in 2011 and 2.13 pg/g lipid in 2018 vs 2.24 pg/g lipid in 2011) seemed to be slightly decreased during 2011–2018 compared to the level from a national study in 2011 (Zhang et al., 2016). This was attributed to the relatively slow annual decline rate of dl-PCBs in breast milk (7.8%, 95% CI: 3.9%–11.5%) (Supplementary Fig. S7B), especially for PCB-126 (not shown). Due to the long half-lives of PCBs (>10 years), the decrease of PCBs in breast milk was slower compared to that of OCPs (Supplementary Table S8). For decreasing EDI of dl-PCBs in a population, continuous surveillance of dl-PCBs in breast milk is critical to evaluate the potential health effects in humans. In addition, a wide research on diet is also necessary, followed by dietary advises for the populations that consume too much of high PCB contaminated food stuff (like seafood) (VKM, 2014). The health effects of PCB exposure have also been extensively studied, and the continuous exposure to PCBs above PTDI levels may cause hepatic (Hardesty et al., 2019), developmental (Winneke et al., 2014), neurobehavioral (Bell, 2014), and immunotoxic effects (Kramer et al., 2012).

4. Limitations

There are many factors that affect the accuracy of the average individual pollutant concentrations in breast milk in the present study, which mainly include geographical distribution signatures, methodological differences, data selection, undetectable congeners, and retrieval time. The geographical distribution signatures were dominated by the area's economic levels and the extent of industrialisation, which were discussed in the previous section. Only the influences of methodological differences, data selection, undetectable congeners, and retrieval time are demonstrated as follow.

In total, the analytical methods for POP determination in breast milk were comparable among different studies. All of the POPs in breast milk were detected with gas chromatography–mass spectrometry (GC–MS), except for PFCs and HBCD diastereoisomer separation, which were mostly detected using liquid chromatography coupled with tandem MS (LC-MS/MS). The methodological differences were mainly in the pre-treatment procedures, which included the selected organic solvents for lipid extraction and the adopted solid phase extraction cartridges for target clean-up.

Because not all of the studies provided the mean, geometric mean, and median values, the estimation of individual pollutant concentrations relied on the different metrics provided in each study. Although mean values were generally selected (Tables S1-S6), bias may exist when using different metrics for calculation. Considering the number of included studies, only the correlations among different metrics of OCP concentrations, PBDE concentrations, and PCB concentrations in breast milk were analysed. The results of the correlation analysis are depicted in Supplementary Fig. S1. Strong correlations existed among different metrics, in accordance with Huang et al.'s conclusion (2017). Therefore, it is relatively appropriate to use different metrics to estimate the average exposure levels in breast milk.

The PFC concentrations in breast milk were relatively low. The average concentrations of perfluorododecanoic acid (PFDoDA) and perfluorotridecanoic acid (PFTrDA) could not be estimated because their concentrations were less than the detection limit in all of the included studies. The total PFC concentration was therefore underestimated. In addition to PFCs, there are also undetectable congeners for other pollutants, but the proportions were negligible. In fact, the average residue level of single POPs in breast milk and its EDI were basically unaffected by undetectable congeners.

We conducted a literature review for studies published from 2001 to 2020. The breast milk sample years varied among different studies, which resulted in relatively higher average concentrations of certain pollutants than reported in national studies. The average EDI of some pollutants (Tables 1-2) and their corresponding HQ values (Fig. 4) may be overestimated in the present study. However, the rank order of HQ values aimed to screen the pollutants with potential risks (Fig. 4), and then a comprehensive health risk for individual pollutants was assessed in detail based on their original studies. The conclusions on the risk assessment of priority pollutants (DDT, HCB, and PCBs) was not affected by the estimated average concentrations.

5. Conclusions

In the present study, we estimated the average levels of individual pollutants in breast milk and then identify the specific POP signatures in samples originating from countrywide regions. To the best of our knowledge, the benefits of breastfeeding far outweigh the toxicological disadvantages of certain POPs. However, we should focus on the dietary POP exposure in the general population, and more steps should be taken to evaluate the health risks for infants exposed to DDT, HCB, and PCBs. The risk assessment of POPs should be strengthened for residents of coastal areas, urban areas, and southern China.

Declaration of competing interest

The authors declare no competing financial interests.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2020.142028.

References

Abdallah, M.A., Harrad, S., 2011. Tetrabromobisphenol-a, hexabromocyclododecane and its degradation products in UK human milk: relationship to external exposure. Environ. Int. 37, 443–448.

Acharya, N., Gautam, B., Subbiah, S., Rogge, M.M., Anderson, T.A., Gao, W., 2019. Polycyclic aromatic hydrocarbons in breast milk of obese vs normal women: infant exposure and risk assessment. Sci. Total Environ. 668, 658–667.

Aerts, R., Van Overmeire, I., Colles, A., Andjelković, M., Malarvannan, G., Poma, G., et al., 2019. Determinants of persistent organic pollutant (POP) concentrations in human breast milk of a cross-sectional sample of primiparous mothers in Belgium. Environ. Int. 131, 104979.

AFSSA–the French Food Safety Agency, 2007. Opinion of the French Food Safety Agency (Afssa) on the establishment of relevant maximum levels for non-dioxin-like polychlorobiphenyls (NDL-PCB) in some foodstuffs. https://www.anses.fr/en/search/site/Opinion%20of%20the%2023rd%20October%202007%20on%20the%20establishment%20of%20relevant%20maximum%20levels%20for%20non%20dioxin-like%20polychlorobiphenyls%20(NDL-PC?iso1=fr&iso2=en.

Al-Saleh, I., Al-Doush, I., Alsabbaheen, A., Mohamed, G.E.D., Rabbah, A., 2012. Levels of DDT and its metabolites in placenta, maternal and cord blood and their potential influence on neonatal anthropometric measures. Sci. Total Environ. 416, 62–74.

Antignac, J.P., Main, K.M., Virtanen, H.E., Boquien, C.Y., Marchand, P., Venisseau, A., et al., 2016. Country-specific chemical signatures of persistent organic pollutants (POPs) in breast milk of French, Danish and Finnish women. Environ. Pollut. 218, 728–738.

Arrebola, J.P., Cuellar, M., Bonde, J.P., González-Alzaga, B., Mercado, L.A., 2016. Associations of maternal o,p'-DDT and p,p'-DDE levels with birth outcomes in a Bolivian cohort. Environ. Res. 151, 469–477.

Asawasinsopon, R., Prapamontol, T., Prakobvitayakit, O., Vaneesorn, Y., Mangklabruks, A., Hock, B., 2006. The association between organochlorine and thyroid hormone levels in cord serum: a study from northern Thailand. Environ. Int. 32, 554–559.

ATSDR–Agency for Toxic Substances and Disease Registry, 2005. Minimal risk levels (MRLs) for hazardous substances. https://www.atsdr.cdc.gov/mrls/mrllist.asp.

Bao, Y., Chi, M., Zhang, L., Meng, G.M., Li, J.G., Zhao, Y.F., et al., 2016. Indicator polychlorinated biphenyls in human milk samples of Beijing in 2014. Chinese. Chin. J. of Public Health Eng. 15, 205–208. https://kns.cnki.net/kns/brief/default_result.aspx.

Bao, Y., Zhang, L., Liu, X., Shi, L., Li, J., Meng, G., et al., 2020. Dioxin-like compounds in paired maternal serum and breast milk under long sampling intervals. Ecotoxicol. Environ. Saf. 194, 110339.

Barbarossa, A., Masetti, R., Gazzotti, T., Zama, D., Astolfi, A., Veyrand, B., et al., 2013. Perfluoroalkyl substances in human milk: a first survey in Italy. Environ. Int. 51, 27–30.

Bedi, J.S., Gill, J.P., Aulakh, R.S., Kaur, P., Sharma, A., Pooni, P.A., 2013. Pesticide residues in human breast milk: risk assessment for infants from Punjab, India. Sci. Total Environ. 463–464, 720–726.

Bell, M.R., 2014. Endocrine-disrupting actions of PCBs on brain development and social and reproductive behaviors. Curr. Opin. Pharmacol. 19, 134–144.

van den Berg, M., Birnbaum, L.S., Denison, M., De Vito, M., Farland, W., Feeley, M., et al., 2006. The 2005 World Health Organization reevaluation of human and mammalian toxic equivalency factors for dioxins and dioxin-like compounds. Toxicol. Sci. 93, 223–241.

van den Berg, M., Kypke, K., Kotz, A., Tritscher, A., Lee, S.Y., Magulova, K., et al., 2017. WHO/UNEP global surveys of PCDDs, PCDFs, PCBs and DDTs in human milk and benefit-risk evaluation of breastfeeding. Arch. Toxicol. 91, 83–96.

Bi, X., Qu, W., Sheng, G., Zhang, W., Mai, B., Chen, D., et al., 2006. Polybrominated diphenyl ethers in South China maternal and fetal blood and breast milk. Environ. Pollut. (Barking, Essex: 1987) 144, 1024–1030.

Bravo, N., Grimalt, J.O., Chashchin, M., Chashchin, V.P., Odland, J.-Ø., 2019. Drivers of maternal accumulation of organohalogen pollutants in Arctic areas (Chukotka, Russia) and 4,4′-DDT effects on the newborns. Environ. Int. 124, 541–552.

Burns, C.J., McIntosh, L.J., Mink, P.J., Jurek, A.M., Li, A.A., 2013. Pesticide exposure and neurodevelopmental outcomes: review of the epidemiologic and animal studies. J. Toxicol. Environ. Health B Crit. Rev. 16, 127–283.

Cao, Y., Harada, K.H., Hitomi, T., Niisoe, T., Wang, P., Shi, Y., et al., 2017. Lactational exposure to short chain chlorinated paraffins in China, Korea, and Japan. Chemosphere 173, 43–48.

Chan, J.K., Xing, G.H., Xu, Y., Liang, Y., Chen, L.X., Wu, S.C., et al., 2007. Body loadings and health risk assessment of polychlorinated dibenzo-p-dioxins and dibenzofurans at an intensive electronic waste recycling site in China. Environ. Sci. Technol. 41, 7668–7674.

Chao, H.R., Wang, S.L., Lin, L.Y., Yu, H.Y., Lu, Y.K., Chou, W.L., et al., 2003. Polychlorinated biphenyls in taiwanese primipara human milk and associated factors. Bull. Environ. Contam. Toxicol. 70, 1097–1103.

Chen, M.W., Santos, H.M., 2018. Association between organochlorine pesticide levels in breast Milk and their effects on female reproduction in a Taiwanese population. Int. J. Environ. Res. Public Health 15, 931–953.

Chen, M.Y., Luo, X.J., Zhang, X.L., He, M.J., Chen, S.J., Mai, B.X., 2011. Chlorinated paraffins in sediments from the Pearl River Delta, South China: spatial and temporal distributions and implication for processes. Environ. Sci. Technol. 45, 9936–9943.

Chen, Z.J., Liu, H.Y., Cheng, Z., Man, Y.B., Zhang, K.S., Wei, W., et al., 2014. Polybrominated diphenyl ethers (PBDEs) in human samples of mother-newborn pairs in South China and their placental transfer characteristics. Environ. Int. 73, 77–84.

Chen, T., Huang, M., Li, J., Li, J., Shi, Z., 2019. Polybrominated diphenyl ethers and novel brominated flame retardants in human milk from the general population in Beijing, China: occurrence, temporal trends, nursing infants' exposure and risk assessment. Sci. Total Environ. 689, 278–286.

Cheng, B., Peng, F.J., Liu, Q.R., Ke, C.L., Liu, Q., Pan, C.G., 2020. Nationwide assessment of persistent halogenated compounds (PHCs) in farmed golden pompano of China. Food Chem. 313, 126135.

Chevrier, J., Rauch, S., Obida, M., Crause, M., Bornman, R., Eskenazi, B., 2019. Sex and poverty modify associations between maternal peripartum concentrations of DDT/E and pyrethroid metabolites and thyroid hormone levels in neonates participating in the VHEMBE study, South Africa. Environ. Int. 131, 104958.

Chovancova, J., Conka, K., Kocan, A., Sejakova, Z.S., 2011. PCDD, PCDF, PCB and PBDE concentrations in breast milk of mothers residing in selected areas of Slovakia. Chemosphere 83, 1383–1390.

Coker, E., Chevrier, J., Rauch, S., Bradman, A., Obida, M., Crause, M., et al., 2018. Association between prenatal exposure to multiple insecticides and child body weight and body composition in the VHEMBE south African birth cohort. Environ. Int. 113, 122–132.

Criswell, R., Lenters, V., Mandal, S., Stigum, H., Iszatt, N., Eggesbø, M., 2017. Persistent environmental toxicants in breast milk and rapid infant growth. Ann. Nutr. metab. 70, 210–216.

Croes, K., Colles, A., Koppen, G., Govarts, E., Bruckers, L., Van de Mieroop, E., et al., 2012. Persistent organic pollutants (POPs) in human milk: a biomonitoring study in rural areas of Flanders (Belgium). Chemosphere 89, 988–994.

Darnerud, P.O., Lignell, S., Glynn, A., Aune, M., Törnkvist, A., Stridsberg, M., 2010. POP levels in breast milk and maternal serum and thyroid hormone levels in mother-child pairs from Uppsala, Sweden. Environ. Int. 36, 180–187.

Darnerud, P.O., Lignell, S., Aune, M., Isaksson, M., Cantillana, T., Redeby, J., et al., 2015. Time trends of polybrominated diphenylether (PBDE) congeners in serum of Swedish mothers and comparisons to breast milk data. Environ. Res. 138, 352–360.

Deng, B., Zhang, J., Zhang, L., Jiang, Y., Zhou, J., Fang, D., et al., 2012. Levels and profiles of PCDD/Fs, PCBs in mothers' milk in Shenzhen of China: estimation of breast-fed infants' intakes. Environ. Int. 42, 47–52.

Devanathan, G., Subramanian, A., Sudaryanto, A., Takahashi, S., Isobe, T., Tanabe, S., 2012. Brominated flame retardants and polychlorinated biphenyls in human breast milk from several locations in India: potential contaminant sources in a municipal dumping site. Environ. Int. 39, 87–95.

Die, Q.Q., Nie, Z.Q., Huang, Q.F., Zhu, X.H., 2014. Organochlorine pesticides (OCPs) in soils of Pearl River Delta, China. J. Agro. Environ. Sci 33, 298–304.

Duan, X., Li, Y., Li, X., Li, M., Zhang, D., 2013. Distributions and sources of polychlorinated biphenyls in the coastal East China Sea sediments. Sci. Total Environ. 463–464, 894–903.

ECB, 2007. European Union Risk Assessment Report, Alkanes, C_{14-17}, Chloro. European Commission, Devon, England https://ec.europa.eu/jrc/en/publication/eur-scientific-and-technical-research-reports/european-union-risk-assessment-report-alkanes-c14-17-chloro-addendum-final-report-2007-risk.

ECB–European Chemicals Bureau, 2008. Updated European Union Risk Assessment Report, Alkanes, C_{10-13}, Chloro. European Commission, Devon, England https://ec.europa.eu/jrc/en/publication/eur-scientific-and-technical-research-reports/updated-european-union-risk-assessment-report-alkanes-c10-13-chloro.

EFSA, 2005. Opinion of the scientific panel on contaminants in the food chain on a request from the commission related to the presence of non-dioxin like polychlorinated biphenyls (PCB) in feed and food. EFSA J. 284, 1–137. https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2005.284.

EFSA, 2008. Opinion of the scientific panel on contaminants in the food chain on Perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA) and their salts. EFSA J. 653, 1–131. https://www.efsa.europa.eu/en/press/news/080721.

EFSA, 2011a. Scientific opinion on Hexabromocyclododecanes (HBCDDs) in food. EFSA J. 9, 2296. https://www.efsa.europa.eu/en/efsajournal/pub/2296.

EFSA, 2011b. Scientific opinion on polybrominated diphenyl ethers (PBDEs) in food. EFSA J. 9, 2156. https://www.efsa.europa.eu/en/efsajournal/pub/2156.

EFSA, 2018. Risk for animal and human health related to the presence of dioxins and dioxin-like PCBs in feed and food. EFSA J. 16, 5333. https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5333.

EFSA–European food safety authority, 2006. Opinion of the Scientific Panel on contaminants in the food chain (CONTAM) related to Hexachlorobenzene as undesirable substance in animal feed. EFSA J. 402, 1–49. https://efsa.onlinelibrary.wiley.com/doi/https://doi.org/10.2903/j.efsa.2006.402.

Eljarrat, E., Guerra, P., Martínez, E., Farré, M., Alvarez, J.G., López-Teijón, M., et al., 2009. Hexabromocyclododecane in human breast milk: levels and enantiomeric patterns. Environ. Sci. Technol. 43, 1940–1946.

Eriksson, P., 1997. Developmental neurotoxicity of environmental agents in the neonate. Neurotoxicology 18, 719–726. https://www.ncbi.nlm.nih.gov/pubmed/9339819.

Erratico, C., Zheng, X., van den Eede, N., Tomy, G., Covaci, A., 2016. Stereoselective metabolism of alpha-, beta-, and gamma-hexabromocyclododecanes (HBCDs) by human liver microsomes and CYP3A4. Environ. Sci. Technol. 50, 8263–8273.

Fang, J., Nyberg, E., Bignert, A., Bergman, A., 2013. Temporal trends of polychlorinated dibenzo-p-dioxins and dibenzofurans and dioxin-like polychlorinated biphenyls in mothers' milk from Sweden, 1972-2011. Environ. Int. 60, 224–231.

Forns, J., Mandal, S., Iszatt, N., Polder, A., Thomsen, C., Lyche, J.L., et al., 2016. Novel application of statistical methods for analysis of multiple toxicants identifies DDT as a risk factor for early child behavioral problems. Environ. Res. 151, 91–100.

Fromme, H., Tittlemier, S.A., Völkel, W., Wilhelm, M., Twardella, D., 2009. Perfluorinated compounds–exposure assessment for the general population in Western countries. Int. J. Hyg. Environ. Health 212, 239–270.

Fromme, H., Mosch, C., Morovitz, M., Alba-Alejandre, I., Boehmer, S., Kiranoglu, M., et al., 2010. Pre- and postnatal exposure to perfluorinated compounds (PFCs). Environ. Sci. Technol. 44, 7123–7129.

Fu, L., Lu, X., Tan, J., Zhang, H., Zhang, Y., Wang, S., et al., 2018. Bioaccumulation and human health risks of OCPs and PCBs in freshwater products of Northeast China. Environ. Pollut. (Barking, Essex: 1987) 242, 1527–1534.

Fujii, Y., Yan, J., Harada, K.H., Hitomi, T., Yang, H., Wang, P., et al., 2012. Levels and profiles of long-chain perfluorinated carboxylic acids in human breast milk and infant formulas in East Asia. Chemosphere 86, 315–321.

Gascon, M., Fort, M., Martínez, D., Carsin, A.E., Forns, J., Grimalt, J.O., et al., 2012. Polybrominated diphenyl ethers (PBDEs) in breast milk and neuropsychological development in infants. Environ. Health Perspect. 120, 1760–1765.

Gebremichael, S., Birhanu, T., Tessema, D.A., 2013. Analysis of organochlorine pesticide residues in human and cow's milk in the towns of Asendabo, Serbo and Jimma in South-Western Ethiopia. Chemosphere 90, 1652–1657.

Govaerts, A., Verhaert, V., Covaci, A., Jaspers, V.L.B., Berg, O.K., Addo-Bediako, A., et al., 2018. Distribution and bioaccumulation of POPs and mercury in the Ga-Selati River (South Africa) and the rivers Gudbrandsdalslågen and Rena (Norway). Environ. Int. 121, 1319–1330.

Grung, M., Lin, Y., Zhang, H., Steen, A.O., Huang, J., Zhang, G., et al., 2015. Pesticide levels and environmental risk in aquatic environments in China–a review. Environ. Int. 81, 87–97.

Haque, R., Inaoka, T., Fujimura, M., Ahmad, A.S., Ueno, D., 2017. Intake of DDT and its metabolites through food items among reproductive age women in Bangladesh. Chemosphere 189, 744–751.

Haraguchi, K., Koizumi, A., Inoue, K., Harada, K.H., Hitomi, T., Minata, M., et al., 2009. Levels and regional trends of persistent organochlorines and polybrominated diphenyl ethers in Asian breast milk demonstrate POPs signatures unique to individual countries. Environ. Int. 35, 1072–1079.

Hardesty, J.E., Wahlang, B., Falkner, K.C., Shi, H., Jin, J., Wilkey, D., Merchant, M., Watson, C., Prough, R.A., Cave, M.C., 2019. Hepatic signalling disruption by pollutant polychlorinated biphenyls in steatohepatitis. Cell. Signal. 53, 132–139.

Hassine, S.B., Ameur, W.B., Gandoura, N., Driss, M.R., 2012. Determination of chlorinated pesticides, polychlorinated biphenyls, and polybrominated diphenyl ethers in human milk from Bizerte (Tunisia) in 2010. Chemosphere 89, 369–377.

Hedley, A.J., Wong, T.W., Hui, L.L., Malisch, R., Nelson, E.A., 2006. Breast milk dioxins in Hong Kong and Pearl River Delta. Environ. Health Perspect. 114, 202–208.

Hong, H., Chen, W., Xu, L., Wang, X., Zhang, L., 1999. Distribution and fate of organochlorine pollutants in the Peral River estuary. Mar. Pollut. Bull. 39, 376–382.

Huang, R.P., Liu, Z.H., Yuan, S.F., Yin, H., Dang, Z., Wu, P.X., 2017. Worldwide human daily intakes of bisphenol A (BPA) estimated from global urinary concentration data (2000-2016) and its risk analysis. Environ. Pollut. 230, 143–152.

Huang, R., Wang, P., Zhang, J., Chen, S., Zhu, P., Huo, W., et al., 2019. The human body burden of polychlorinated dibenzo-p-dioxins/furans (PCDD/fs) and dioxin-like polychlorinated biphenyls (DL-PCBs) in residents' human milk from Guangdong Province, China. Toxicol. Res. (Camb). 8, 552–559.

Iszatt, N., Janssen, S., Lenters, V., Dahl, C., Stigum, H., Knight, R., et al., 2019. Environmental toxicants in breast milk of Norwegian mothers and gut bacteria composition and metabolites in their infants at 1 month. Microbiome 7, 34.

Jian, J.M., Guo, Y., Zeng, L., Liang, Y.L., Lu, X., Wang, F., et al., 2017. Global distribution of perfluorochemicals (PFCs) in potential human exposure source-a review. Environ. Int. 108, 51–62.

Jin, J., Wang, Y., Yang, C., Hu, J., Liu, W., Cui, J., et al., 2009. Polybrominated diphenyl ethers in the serum and breast milk of the resident population from production area, China. Environ. Int. 35, 1048–1052.

Johansson, N., Fredriksson, A., Eriksson, P., 2008. Neonatal exposure to perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) causes neurobehavioural defects in adult mice. Neurotoxicology 29, 160–169.

Johnson-Restrepo, B., Addink, R., Wong, C., Arcaro, K., Kannan, K., 2007. Polybrominated diphenyl ethers and organochlorine pesticides in human breast milk from Massachusetts, USA. J. Environ. Monit. 9, 1205–1212.

Kao, C.C., Que, D.E., Bongo, S.J., Tayo, L.L., Lin, Y.H., Lin, C.W., et al., 2019. Residue levels of organochlorine pesticides in breast milk and its associations with cord blood thyroid hormones and the offspring's neurodevelopment. Int. J. Environ. Res. Public Health 16, 1438.

Karrman, 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, 226–230.

Kim, S., Choi, K., Ji, K., Seo, J., Kho, Y., Park, J., et al., 2011. Trans-placental transfer of thirteen perfluorinated compounds and relations with fetal thyroid hormones. Environ. Sci. Technol. 45, 7465–7472.

Kishikawa, N., Kuroda, N., 2009. Evaluation of organic environmental pollutants detected in human milk. J. Heal. Sci. 55, 1–10.

Kramer, S., Hikel, S.M., Adams, K., Hinds, D., Moon, K., 2012. Current status of the epidemiologic evidence linking polychlorinated biphenyls and non-hodgkin lymphoma, and the role of immune dysregulation. Environ. Health Perspect. 120, 1067–1075.

Kuang, L., Hou, Y., Huang, F., Hong, H., Sun, H., Deng, W., et al., 2020. Pesticide residues in breast milk and the associated risk assessment: a review focused on China. Sci. Total Environ. 727, 138412.

Kunisue, T., Muraoka, M., Ohtake, M., Sudaryanto, A., Minh, N.H., Ueno, D., et al., 2006. Contamination status of persistent organochlorines in human breast milk from Japan: recent levels and temporal trend. Chemosphere 64, 1601–1608.

Kyriklaki, A., Vafeiadi, M., Kampouri, M., Koutra, K., Roumeliotaki, T., Chalkiadaki, G., et al., 2016. Prenatal exposure to persistent organic pollutants in association with offspring neuropsychological development at 4 years of age: the Rhea mother-child cohort, Crete, Greece. Environ. Int. 97, 204–211.

Lee, S., Kim, S., Park, J., Kim, H.J., Choi, G., Choi, S., et al., 2018. Perfluoroalkyl substances (PFASs) in breast milk from Korea: time-course trends, influencing factors, and infant exposure. Sci. Total Environ. 612, 286–292.

Lehmann, G.M., Verner, M.A., Luukinen, B., Henning, C., Assimon, S.A., LaKind, J.S., et al., 2014. Improving the risk assessment of lipophilic persistent environmental chemicals in breast milk. Crit. Rev. Toxicol. 44, 600–617.

Leng, J.H., Kayama, F., Wang, P.Y., Nakamura, M., Nakata, T., Wang, Y., 2009. Levels of persistent organic pollutants in human milk in two Chinese coastal cities, Tianjin and Yantai: influence of fish consumption. Chemosphere 75, 634–639.

Lenters, V., Iszatt, N., Forns, J., Cechova, E., Kocan, A., Legler, J., et al., 2019. Early-life exposure to persistent organic pollutants (OCPs, PBDEs, PCBs, PFASs) and attention-deficit/hyperactivity disorder: a multi-pollutant analysis of a Norwegian birth cohort. Environ. Int. 125, 33–42.

Li, Q.B., Zhang, H., Luo, Y.M., Song, J., Wu, L.H., Ma, J.M., 2008. Residues of DDTs and their spatial distribution characteristics in soils from the Yangtze River Delta, China. Environ. Toxicol. Chem. (1), 24–30.

Li, J., Zhang, L., Wu, Y., Liu, Y., Zhou, P., Wen, S., et al., 2009. A national survey of polychlorinated dioxins, furans (PCDD/Fs) and dioxin-like polychlorinated biphenyls (dl-PCBs) in human milk in China. Chemosphere 75, 1236–1242.

Li, C., Cheng, Y., Tang, Q., Lin, S., Li, Y., Hu, X., et al., 2014. The association between prenatal exposure to organochlorine pesticides and thyroid hormone levels in newborns in Yancheng, China. Environ. Res. 129, 47–51.

Li, Z.M., Albrecht, M., Fromme, H., Schramm, K.W., De Angelis, M., 2020. Persistent organic pollutants in human breast milk and associations with maternal thyroid hormone homeostasis. Environ. Sci. Technol. 54, 1111–1119.

Lignell, S., Winkvist, A., Bertz, F., Rasmussen, K.M., Glynn, A., Aune, M., et al., 2016. Environmental organic pollutants in human milk before and after weight loss. Chemosphere 159, 96–102.

Liu, J., Li, J., Zhao, Y., Wang, Y., Zhang, L., Wu, Y., 2010. The occurrence of perfluorinated alkyl compounds in human milk from different regions of China. Environ. Int. 36, 433–438.

Liu, J., Li, J., Liu, Y., Chan, H.M., Zhao, Y., Cai, Z., et al., 2011. Comparison on gestation and lactation exposure of perfluorinated compounds for newborns. Environ. Int. 37, 1206–1212.

Liu, Y., Aamir, M., Li, M., Liu, K., Hu, Y., Liu, N., et al., 2020. Prenatal and postnatal exposure risk assessment of chlorinated paraffins in mothers and neonates: occurrence, congener profile, and transfer behavior. J. Hazard. Mater. 395, 122660.

Lu, D., Wang, D., Ni, R., Lin, Y., Feng, C., Xu, Q., et al., 2015a. Organochlorine pesticides and their metabolites in human breast milk from Shanghai, China. Environ. Sci. Pollut. Res. Int. 22, 9293–9306.

Lu, D., Lin, Y., Feng, C., Wang, D., She, J., Shen, H., Wang, G., Zhou, Z., 2015b. Levels of polychlorinated dibenzo-p-dioxins/furans (PCDD/Fs) and dioxin-like polychlorinated biphenyls (DL-PCBs) in breast milk in Shanghai, China: a temporal upward trend. Chemosphere 137, 14–24.

Lu, S., Tan, Z., Jiang, Y., Wu, D., Zhang, J., Zhou, J., Lin, X., 2018. Hexabromocyclododecanes in breast milk from residents in Shenzhen, China: implications for infant exposure. Sci. Total Environ. 622-623, 1090–1097.

Mamontova, E.A., Tarasova, E.N., Mamontov, A.A., 2017. PCBs and OCPs in human milk in eastern Siberia, Russia: levels, temporal trends and infant exposure assessment. Chemosphere 178, 239–248.

Mariussen, E., Fonnum, F., 2006. Neurochemical targets and behavioral effects of organohalogen compounds: an update. Crit. Rev. Toxicol. 36, 253–289.

Meng, J., Hong, S., Wang, T., Li, Q., Yoon, S.J., Lu, Y., et al., 2017. Traditional and new POPs in environments along the Bohai and Yellow Seas: An overview of China and South Korea. Chemosphere 169, 503–515.

Mostafalou, S., 2016. Persistent organic pollutants and concern over the link with insulin resistance related metabolic diseases. Rev. Environ. Contam. Toxicol. 238, 69–89.

Motas Guzmàn, M., Clementini, C., Pérez-Cárceles, M.D., Jiménez Rejón, S., Cascone, A., Martellini, T., et al., 2016. Perfluorinated carboxylic acids in human breast milk from Spain and estimation of infant's daily intake. Sci. Total Environ. 544, 595–600.

van Mourik, L.M., Gaus, C., Leonards, P.E.G., de Boer, J., 2016. Chlorinated paraffins in the environment: a review on their production, fate, levels and trends between 2010 and 2015. Chemosphere 155, 415–428.

Muller, M.H.B., Polder, A., Brynildsrud, O.B., Karimi, M., Lie, E., Manyilizu, W.B., et al., 2017. Organochlorine pesticides (OCPs) and polychlorinated biphenyls (PCBs) in human breast milk and associated health risks to nursing infants in northern Tanzania. Environ. Res. 154, 425–434.

Muller, M.H.B., Polder, A., Brynildsrud, O.B., Grønnestad, R., Karimi, M., Lie, E., et al., 2019. Prenatal exposure to persistent organic pollutants in northern Tanzania and their distribution between breast milk, maternal blood, placenta and cord blood. Environ. Res. 170, 433–442.

National Health Commission of the People''s Republic of China, 2019. National Food Safety Standard-Maximum Residue Limits for Pesticides in Food (GB 2673–2019). China Agriculture Press, Beijing.

Needham, L.L., Grandjean, P., Heinzow, B., Jørgensen, P.J., Nielsen, F., Patterson, D.G., et al., 2011. Partition of environmental chemicals between maternal and fetal blood and tissues. Environ. Sci. Technol. 45, 1121–1126.

Ni, K., Lu, Y., Wang, T., Kannan, K., Gosens, J., Xu, L., et al., 2013. A review of human exposure to polybrominated diphenyl ethers (PBDEs) in China. Int. J. Hyg. Environ. Health 216, 607–623.

Polder, A., Gabrielsen, G.W., Odland, J.O., Savinova, T.N., Tkachev, A., Loken, K.B., et al., 2008. Spatial and temporal changes of chlorinated pesticides, PCBs, dioxins (PCDDs/PCDFs) and brominated flame retardants in human breast milk from northern Russia. Sci. Total Environ. 391, 41–54.

Rawn, D.F.K., Sadler, A.R., Casey, V.A., Breton, F., Sun, W.F., Arbuckle, T.E., et al., 2017. Dioxins/furans and PCBs in Canadian human milk: 2008-2011. Sci. Total Environ. 595, 269–278.

Ryan, J.J., Rawn, D.F.K., 2014. The brominated flame retardants, PBDEs and HBCD, in Canadian human milk samples collected from 1992 to 2005; concentrations and trends. Environ. Int. 70, 1–8.

Saeedi Saravi, S.S., Dehpour, A.R., 2016. Potential role of organochlorine pesticides in the pathogenesis of neurodevelopmental, neurodegenerative, and neurobehavioral disorders: a review. Life Sci. 145, 255–264.

Shen, H., Ding, G., Wu, Y., Pan, G., Zhou, X., Han, J., Li, J., Wen, S., 2012. Polychlorinated dibenzo-p-dioxins/furans (PCDD/Fs), polychlorinated biphenyls (PCBs), and polybrominated diphenyl ethers (PBDEs) in breast milk from Zhejiang, China. Environ. Int. 42, 84–90.

Shi, Z.X., Wu, Y.N., Li, J.G., Zhao, Y.F., Feng, J.F., 2009. Dietary exposure assessment of Chinese adults and nursing infants to tetrabromobisphenol-A and hexabromocyclododecanes: occurrence measurements in foods and human milk. Environ. Sci. Technol. 43, 4314–4319.

Shi, R.J., Zhong, Y.T., Lei, Y.X., Zhang, J.X., Li, X.N., Jiang, Y.X., et al., 2013. Accumulative levels of organochlorine pesticides of HCHs, DDTs in breast milk and risk factors analysis in Shenzhen (in Chinese). Wei Sheng Yan Jiu 42, 205–210.

Shi, Z., Zhang, L., Zhao, Y., Sun, Z., Zhou, X., Li, J., et al., 2017a. A national survey of tetrabromobisphenol-A, hexabromocyclododecane and decabrominated diphenyl ether in human milk from China: occurrence and exposure assessment. Sci. Total Environ. 599–600, 237–245.

Shi, Z., Zhang, L., Zhao, Y., Sun, Z., Zhou, X., Li, J., et al., 2017b. Dietary exposure assessment of Chinese population to tetrabromobisphenol-A, hexabromocyclododecane and decabrominated diphenyl ether: results of the 5th Chinese Total diet study. Environ. Pollut. 229, 539–547 (Barking, Essex: 1987).

Shi, Z., Zhang, L., Li, J., Wu, Y., 2018. Legacy and emerging brominated flame retardants in China: a review on food and human milk contamination, human dietary exposure and risk assessment. Chemosphere 198, 522–536.

So, M.K., Miyake, Y., Yeung, W.Y., Ho, Y.M., Taniyasu, S., Rostkowski, P., et al., 2007. Perfluorinated compounds in the Pearl River and Yangtze River of China. Chemosphere 68, 2085–2095.

Solomon, G.M., Weiss, P.M., 2002. Chemical contaminants in breast milk: time trends and regional variability. Environ. Health Perspect. 110.

Song, S., Ma, X., Tong, L., Tian, Q., Huang, Y., Yin, S., et al., 2013. Residue levels of hexachlorocyclohexane and dichlorodiphenyltrichloroethane in human milk collected from Beijing. Environ. Monit. Assess. 185, 7225–7229.

Song, X., Vestergren, R., Shi, Y., 2018. Emissions, transport, and fate of emerging per- and polyfluoroalkyl substances from one of the major fluoropolymer manufacturing facilities in China. Environ. Sci. Technol. 52, 9694–9703.

Stigum, H., Iszatt, N., Polder, A., Mandal, S., Eggesbø, M., 2015. A novel model to characterize postnatal exposure to lipophilic environmental toxicants and application in the study of hexachlorobenzene and infant growth. Environ. Int. 85, 156–162.

Subramanian, A., Ohtake, M., Kunisue, T., Tanabe, S., 2007. High levels of organochlorines in mothers' milk from Chennai (Madras) city, India. Chemosphere 68, 928–939.

Sun, S.J., Kayama, F., Zhao, J.H., Ge, J., Yang, Y.X., Fukatsu, H., et al., 2011. Longitudinal increases in PCDD/F and dl-PCB concentrations in human milk in northern China. Chemosphere 85, 448–453.

Tang, D., Liu, X., He, H., Cui, Z., Gan, H., Xia, Z., 2020. Distribution, sources and ecological risks of organochlorine compounds (DDTs, HCHs and PCBs) in surface sediments from the Pearl River Estuary, China. Mar. Pollut. Bull. 152, 110942.

Tao, L., Ma, J., Kunisue, T., Libelo, E.L., Tanabe, S., Kannan, K., 2008a. Perfluorinated compounds in human breast milk from several Asian countries, and in infant formula and dairy milk from the United States. Environ. Sci. Technol. 42, 8597–8602.

Tao, L., Kannan, K., Wong, C.M., Arcaro, K.F., Butenhoff, J.L., 2008b. Perfluorinated compounds in human milk from Massachusetts, U.S.a. Environ. Sci. Technol. 42, 3096–3101.

Tao, S., Yu, Y., Liu, W., Wang, X., Cao, J., Li, B., et al., 2008c. Validation of dietary intake of dichlorodiphenyltrichloroethane and metabolites in two populations from Beijing and Shenyang, China based on the residuals in human milk. Environ. Sci. Technol. 42, 7709–7714.

Thomas, G.O., Farrar, D., Braekevelt, E., Stern, G., Kalantzi, O.I., Martin, F.L., et al., 2006. Short and medium chain length chlorinated paraffins in UK human milk fat. Environ. Int. 32, 34–40.

Thomsen, C., Stigum, H., Froshaug, M., Broadwell, S.L., Becher, G., Eggesbo, M., 2010. Determinants of brominated flame retardants in breast milk from a large scale Norwegian study. Environ. Int. 36, 68–74.

Toms, L.M., Guerra, P., Eljarrat, E., Barcelo, D., Harden, F.A., Hobson, P., et al., 2012. Brominated flame retardants in the Australian population: 1993–2009. Chemosphere 89, 398–403.

Tsydenova, O.V., Sudaryanto, A., Kajiwara, N., Kunisue, T., Batoev, V.B., Tanabe, S., 2007. Organohalogen compounds in human breast milk from Republic of Buryatia, Russia. Environ. Pollut. (Barking, Essex: 1987) 146, 225–232.

Tue, N.M., Sudaryanto, A., Minh, T.B., Isobe, T., Takahashi, S., Viet, P.H., Tanabe, S., 2010. Accumulation of polychlorinated biphenyls and brominated flame retardants in breast milk from women living in Vietnamese e-waste recycling sites. Sci. Total Environ. 408, 2155–2162.

UNEP, 2001. The 12 initial POPs under the Stockholm convention. http://chm.pops.int/TheConvention/ThePOPs/The12InitialPOPs/tabid/296/Default.aspx.

UNEP, 2009. The new POPs under the Stockholm convention. http://chm.pops.int/TheConvention/ThePOPs/TheNewPOPs/tabid/2511/Default.aspx.

UNEP, 2013. Results of the global survey on concentrations in human milk of persistent organic pollutants by the United Nations environment programme and the World Health Organization. Conference of the Parties to the Stockholm Convention on Persistent Organic Pollutants Sixth Meeting. Geneva, 28 April —10 May 2013.

UNEP, 2017. The new POPs under the Stockholm convention. http://chm.pops.int/TheConvention/ThePOPs/TheNewPOPs/tabid/2511/Default.aspx.

UNEP–United Nations Environment Programme, 2001. Final Act of the Conference of Plenipotentiaries on the Stockholm Convention on Persistent Organic Pollutants Stockholm. United Nations Environment Programme.

USEPA, 1987. Gamma-Hexachlorocyclohexane (γ-HCH), CASRN 58-89-9 integrated risk information system (IRIS) chemical assessment summary. https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?&substance_nmbr=65.

USEPA, 2010. EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments. United States Environmental Protection Agency. United States Environmental Protection Agency, Washington DC.

USEPA–United States Environmental Protection Agency, 1987. p,p'-Dichlorodiphenyltrichloroethane (DDT), CASRN 50-29-3. Integrated risk information system (IRIS) chemical assessment summary. https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=147.

VKM, 2014. Benefit-Risk Assessment of Fish and Fish Products in the Norwegian Diet-an Update. vol. 15. Scientific Opinion of the Scientific Steering Committee, Oslo, Norway [293 pp], ISBN: 978-82-8259-159-1. https://vkm.no/download/18.2994e95b15cc54507161ea1a/1498222018046/0a646edc5e.pdf.

Wang, G., Lu, Y., Han, J., et al., 2010a. Hexachlorobenzene sources, levels and human exposure in the environment of China. Environ. Int. 36, 122–130.

Wang, N., Kong, D., Cai, D., Shi, L., Cao, Y., Pang, G., et al., 2010b. Levels of polychlorinated biphenyls in human adipose tissue samples from Southeast China. Environ. Sci. Technol. 44, 4334–4340.

Wang, Y., Li, J., Cheng, Z., Li, Q., Pan, X., Zhang, R., et al., 2013. Short- and medium-chain chlorinated paraffins in air and soil of subtropical terrestrial environment in the pearl river delta, South China: distribution, composition, atmospheric deposition fluxes, and environmental fate. Environ. Sci. Technol 47, 2679–2687.

Wang, T., Wang, P., Meng, J., Liu, S., Lu, Y., Khim, J.S., et al., 2015. A review of sources, multimedia distribution and health risks of perfluoroalkyl acids (PFAAs) in China. Chemosphere 129, 87–99.

Wang, X., Gong, P., Wang, C., Ren, J., Yao, T., 2016a. A review of current knowledge and future prospects regarding persistent organic pollutants over the Tibetan Plateau. Sci. Total Environ. 573, 139–154.

Wang, T., Vestergren, R., Herzke, D., Yu, J., Cousins, I.T., 2016b. Levels, isomer profiles, and estimated riverine mass discharges of perfluoroalkyl acids and fluorinated alternatives at the mouths of Chinese Rivers. Environ. Sci. Technol. 50, 11584–11592.

Wang, J., Zhao, X., Wang, Y., Shi, Z., 2019. Tetrabromobisphenol A, hexabromocyclododecaneisomers and polybrominated diphenyl ethers in foodstuffs from Beijing, China: contamination levels, dietary exposure and risk assessment. Sci. Total Environ. 666, 812–820.

Weber, R., Bell, L., Watson, A., Petrlik, J., Paun, M.C., Vijgen, J., 2019. Assessment of pops contaminated sites and the need for stringent soil standards for food safety for the protection of human health. Environ. Pollut. (Barking, Essex: 1987) 249, 703–715.

WHO–World Health Organization, d. Persistent organic pollutants (POPs). [Cited 2020 Jun 29]. https://www.who.int/foodsafety/areas_work/chemical-risks/pops/en/.

Winneke, G., Ranft, U., Wittsiepe, J., Kasper-Sonnenberg, M., Fürst, P., Krämer, U., et al., 2014. Behavioral sexual dimorphism in school-age children and early developmental exposure to dioxins and PCBs: a follow-up study of the Duisburg cohort. Environ. Health Perspect. 122, 292–298.

Wittsiepe, J., Fürst, P., Schrey, P., Lemm, F., Kraft, M., Eberwein, G., et al., 2007. PCDD/F and dioxinlike PCB in human blood and milk from German mothers. Chemosphere 67, S286–S294.

Wohlfahrt-Veje, C., Audouze, K., Brunak, S., Antignac, J.P., le Bizec, B., Juul, A., et al., 2014. Polychlorinated dibenzo-p-dioxins, furans, and biphenyls (PCDDs/PCDFs and PCBs) in breast milk and early childhood growth and IGF1. Reproduction 147, 391–399.

Wong, C.K., Leung, K.M., Poon, B.H., Lan, C.Y., Wong, M.H., 2002. Organochlorine hydrocarbons in human breast milk collected in Hong Kong and Guangzhou. Arch. Environ. Contam. Toxicol. 43, 364–372.

Wong, M.H., Leung, A.O., Chan, J.K., Choi, M.P., 2005. A review on the usage of POP pesticides in China, with emphasis on DDT loadings in human milk. Chemosphere 60, 740–752.

Wong, T.W., Wong, A.H.S., Nelson, E.A.S., Qiu, H., Ku, S.Y.K., 2013. Levels of PCDDs, PCDFs, and dioxin-like PCBs in human milk among Hong Kong mothers. Sci. Total Environ. 463–464, 1230–1238.

Wu, Z., He, C., Han, W., Song, J., Li, H., Zhang, Y., et al., 2020. Exposure pathways, levels and toxicity of polybrominated diphenyl ethers in humans: a review. Environ. Res. 187, 109531.

Xia, D., Gao, L.R., Zheng, M.H., Li, J.G., Zhang, L., Wu, Y.N., et al., 2016. Human exposure to short- and medium-chain chlorinated paraffins via mothers' milk in Chinese urban population. Environ. Sci. Technol 51, 608–615.

Xia, D., Gao, L.R., Zheng, M.H., Li, J.G., Zhang, L., Wu, Y.N., et al., 2017. Health risks posed to infants in rural China by exposure to short- and medium-chain chlorinated paraffins in breast milk. Environ. Int. 103, 1–7.

Xu, C., Tang, M., Zhang, H., Zhang, C., Liu, W., 2016. Levels and patterns of DDTs in maternal colostrum from an island population and exposure of neonates. Environ. Pollut. 209, 132–139.

Xu, C., Yin, S., Tang, M., Liu, K., Yang, F., Liu, W., 2017. Environmental exposure to DDT and its metabolites in cord serum: distribution, enantiomeric patterns, and effects on infant birth outcomes. Sci. Total Environ. 580, 491–498.

Yu, S.Y., Liu, W.J., Xu, Y.S., Zhao, Y.Z., Cai, C.Y., Liu, Y., et al., 2019. Organochlorine pesticides in ambient air from the littoral cities of northern China: spatial distribution, seasonal variation, source apportionment and cancer risk assessment. Science Total Environ 652, 163–176.

Zegers, B.N., Mets, A., Van Bommel, R., Minkenberg, C., Hamers, T., Kamstra, J.H., et al., 2005. Levels of hexabromocyclododecane in harbor porpoises and common dolphins from western European seas, with evidence for stereoisomer-specific biotransformation by cytochrome P450. Environ. Sci. Technol. 39, 2095–2100.

Zeng, L., Lam, J.C., Wang, Y., Jiang, G., Lam, P.K., 2015. Temporal trends and pattern changes of short- and medium-chain chlorinated paraffins in marine mammals from the South China Sea over the past decade. Environ. Sci. Technol. 49, 11348–11355.

Zeng, L., Lam, J.C.W., Horii, Y., Li, X., Chen, W., Qiu, J.W., et al., 2017. Spatial and temporal trends of short- and medium-chain chlorinated paraffins in sediments off the urbanized coastal zones in China and Japan: a comparison study. Environ. Pollut. (Barking, Essex: 1987) 224, 357–367.

Zhang, L., Li, J., Zhao, Y., Li, X., Yang, X., Wen, S., et al., 2011. A national survey of polybrominated diphenyl ethers (PBDEs) and indicator polychlorinated biphenyls (PCBs) in Chinese mothers' milk. Chemosphere 84, 625–633.

Zhang, J.G., Sun, X.W., Ai, H., 2012a. Levels and congener profiles of polybrominated diphenyl ethers (PBDEs) in primipara breast milk from Shenzhen and exposure risk for breast-fed infants. J. Environ. Monit. 14, 893–900.

Zhang, A.P., Chen, Z.Y., Ahrens, L., Liu, W.P., Li, Y.F., 2012b. Concentrations of DDTs and enantiomeric fractions of chiral DDTs in agricultural soils from Zhejiang Province, China, and correlations with total organic carbon and pH. J. Agr. Food Chem. 60, 8294–8301.

Zhang, L., Yin, S., Li, J., Zhao, Y., Wu, Y., 2016. Increase of polychlorinated dibenzo-p-dioxins and dibenzofurans and dioxin-like polychlorinated biphenyls in human milk from China in 2007–2011. Int. J. Hyg. Environ. Health 219, 843–849.

Zhang, L., Yin, S., Zhao, Y., Shi, Z., Li, J., Wu, Y., 2017a. Polybrominated diphenyl ethers and indicator polychlorinated biphenyls in human milk from China under the Stockholm convention. Chemosphere 189, 32–38.

Zhang, Q., Xia, Z., Wu, M., Wang, L., Yang, H., 2017b. Human health risk assessment of DDTs and HCHs through dietary exposure in Nanjing, China. Chemosphere 177, 211–216.

Zhou, Y., Yuan, B., 2020. Chlorinated Paraffins in human Milk from urban sites in China, Sweden, and Norway. Environ. Sci. Technol. 54, 4356–4366.

Zhou, P., Wu, Y., Yin, S., Li, J., Zhao, Y., Zhang, L., et al., 2011. National survey of the levels of persistent organochlorine pesticides in the breast milk of mothers in China. Environ. Pollut. 159, 524–531.

Zhou, J., Zeng, X., Zheng, K., Zhu, X., Ma, L., Xu, Q., et al., 2012a. Musks and organochlorine pesticides in breast milk from Shanghai, China: levels, temporal trends and exposure assessment. Ecotoxicol. Environ. Saf. 84, 325–333.

Zhou, X.P., Shao, P.G., Long, H.J., Ming, X.X., Tao, S.H., Li, C., et al., 2012b. Accumulative level and trend analysis of organochlorine pesticides in the breast milk in Shaoxing. Chinese. Chinese J. Health Lab. Technol. 22, 953–954+959. https://kns.cnki.net/kns/brief/default_result.aspx.

Zhou, S.S., Tang, Q.Z., Jin, M.Q., Liu, W.P., Niu, L.L., Ye, H., 2014. Residues and chiral signatures of organochlorine pesticides in mollusks from the coastal regions of the Yangtze River Delta: source and health risk implication. Chemosphere 114, 40–50.

Zhuo, M., Ma, S., Li, G., Yu, Y., An, T., 2019. Chlorinated paraffins in the indoor and outdoor atmospheric particles from the Pearl River Delta: characteristics, sources, and human exposure risks. Sci. Total Environ. 650, 1041–1049.