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Time trends of persistent organic pollutants in 30 year olds sampled in 1986, 1994, 2001 and 2007 in Northern Norway: Measurements, mechanistic modeling and a comparison of study designs

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ABSTRACT

Background: Human biomonitoring studies have demonstrated decreasing concentrations of many persistent organic pollutants (POPs) in years after emission peaks.
Objectives: To describe time trends of POPs in blood using four cross-sectional samples of 30 year olds from Tromsø, Norway across 1986–2007, and to compare the measured concentrations of polychlorinated biphenyl 153 (PCB-153) to model-estimated values. A second objective was to compare the repeated cross-sectional time trends with those observed in our previous longitudinal study using repeated individual measurements in older men from the same surveys.
Methods: Serum from 45 persons aged 30 years in each of the following years: 1986, 1994, 2001, and 2007 was analyzed for 14 POPs. Further, predicted concentrations of PCB-153 in each sampling year were derived using the emission-based CoZMoMAN model.
Results: The median decreases in summed serum POP concentrations (lipid-adjusted) in 1994, 2001, and 2007 relative to 1986 were − 71%, − 81%, and − 86% for women and − 65%, − 77%, and − 87% for men, respectively. The overall time trend in predicted PCB-153 concentrations demonstrated agreement with the observed trend although model predictions were higher than the measured concentrations at all time points. Compared to our previous longitudinal study of repeated individual measurements in older men, similar although more prominent declines were observed in the younger cross-sectional samples.
Discussion: Observed declines in serum concentrations from 1986 to 2007 were substantial for legacy POPs in men and women at reproductive ages in Northern Norway and are generally consistent with previous longitudinal biomonitoring efforts in the study population. The measured concentrations and observed declines likely reflect a combination of recent and historic exposures. Small differences in time trends observed between the studies could be attributed to different study designs (i.e. the chosen age group or sex and cross-sectional versus repeated individual measurement sampling).

1. Introduction

Biomonitoring of persistent organic pollutants (POPs) in humans has demonstrated decreasing concentrations of POPs for which historic production and use have been restricted or banned in national and international efforts. For example, concentrations of polychlorinated biphenyls (PCBs) and many organochlorine pesticides have decreased in human blood in many 'western countries' since the 1980s (Hagmar et al., 2006; Hovinga et al., 1992; Høyer et al., 2000; Tee et al., 2003; Vo et al., 2008). In our previous longitudinal study of five repeated individual measurements of serum POP concentrations in 53 men from Northern Norway, we demonstrated decreasing concentrations of many

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legacy POPs from 1979 to 2007 (Nøst et al., 2013). Our results also suggested that earlier born birth cohorts had higher concentrations of legacy POPs compared to later born cohorts. Overall, observed time trends in human biomonitoring studies demonstrate the link with trends in environmental emissions (the sum of environmental releases across the chemical life cycle; manufacturing, use and disposal stages) (Nøst et al., 2017). Indeed, the observed trends for PCBs in blood in the longitudinal study was in agreement with those predicted by time-variant mechanistic modeling that was based on historic emissions and published data on environmental fate and human bioaccumulation (Nøst et al., 2013, 2017). In summary, changes in human exposure to POPs across calendar years reflect changes in emissions, environmental concentrations and dietary intakes.

The interdependence of age, period, and cohort effects produces mutual confounding in time-trend studies (Glenn, 2003). As age was confounded by periodic changes in the previous longitudinal study, the blood POP trends were decreasing as the men aged (Nøst et al., 2013), which is in apparent contrast to the positive associations observed between age and concentrations of several legacy POPs in many cross-sectional studies (e.g. Hardell et al., 2010; Wolff et al., 2005). Thus, in order to further expand our knowledge of human time trends of POPs and the relevance of age-period-cohort effects to the interpretation of human biomonitoring, the present study was based on repeated cross-sectional samples of 30 year olds in the same population surveys from Tromsø, Norway as in our previous longitudinal study using repeated individual measurements. This allowed us to extract information on changing human concentrations in reproductively active ages while using repeated cross-sectional sampling from the same population surveys over a time-period of 22 years. Finally, we aimed to evaluate the agreement of measured concentrations of PCB-153 and predicted concentrations from an emission-based mechanistic exposure model as previously used.

2. Materials and methods

2.1. Study population and subject selection

The basis of this study is repeated population surveys in the municipality of Tromsø in Northern Norway where over 40,000 people have participated (summarized by Jacobsen et al., 2012). We used samples from the surveys conducted in 1986–1987 (hereafter referred to as 1986), 1994–1995 (1994), 2001, and 2007–2008 (2007). For each survey, 45 subjects at the age of 30 at the time of the survey were randomly selected (samples from the 2007 survey included 30 and 31 year olds). In total, the present analyses were comprised of 180 serum samples. Both sexes at the age of 30 were chosen to represent an age group that is within reproductive ages. Birth year and body mass index information was extracted from questionnaires.

The study was approved by the Regional Committees for Medical Research Ethics. Participation was voluntary and all participants provided informed consent. Serum samples were stored at −70 °C until they were shipped frozen for analyses.

2.2. Analytical methodology

All POP analyses were performed in 2016 at the Centre de toxicologie du Québec (CTQ), Institut National de Santé Publique du Québec (INSPQ), Québec, Canada. Serum samples were extracted and analyzed for hexachlorobenzene (HCB); *oxy*-chlordane; PCB congeners 52, 101, 118, 153, 156, 170, and 180; *p,p′*-dichlorodiphenyldichloroehylene (*p,p′*-DDE); *p,p′*-dichlorophenyltrichloroethane (*p,p′*-DDT); *β*- hexachlorohexane (*β*-HCH) and *trans*-nonachlor. In short, 0.5–1 mL serum samples were extracted using hexane and saturated ammonium sulphate solution. The extracts were cleaned up using Florisil columns before analyzed using gas chromatography coupled to a mass spectrometer operating in electron capture negative ionization. Certified reference materials and blank samples were analyzed along with the samples. The method is described in detail by Fisher et al. (2016). Mean recoveries of internal standards were 98%, 79%, 114%, 104% for the 1986, 1994, 2001, and 2007 samples, respectively.

2.3. Lipid determinations

Concentrations of total cholesterol (CHOL) and triglycerides (TG) were available from analyses at the time of blood sampling. The methods for determination are described by Wilsgaard et al. (2001) for samples from 1986 and 1994, by Hartz et al. (2004) for samples from 2001, and by Johnsen et al. (2011) for samples from 2007. The concentrations were summed according to the formula by Covaci et al. (2006):

$$\text{Total lipid(TL)} = 1.33*\text{TG} + 1.12*\text{CHOL} + 1.48\,(\text{g/L})$$

2.4. Time-variant model simulations of PCBs in serum

Simulations of lipid-normalized serum concentrations of PCB-153 in 1986, 1994, 2001, and 2007 were carried out using the time-variant multimedia mechanistic CoZMoMAN model (Breivik et al., 2010). Simulations were performed assuming time-variant emission scenarios (Quinn et al., 2011). In general, model parameters were set as outlined by Breivik et al. (2010) and further described in Nøst et al. (2013). Specifically, trends and concentrations in the environment in Northern Norway were assumed similar to those of western areas of the Baltic sea drainage basin, including Sweden and areas in southeastern Norway, as in the model development. Dietary input parameters were selected as described for the average Norwegian fish consumption by Nøst et al. (2013). Model predictions for PCB-153 were obtained for the birth years 1956, 1964, 1971, and 1977 corresponding to those of the study participants. All model calculations assumed that fish consumption was equal among the birth cohorts and two scenarios of fish consumption were considered. Fish consumption rates were either assumed corresponding to the average Norwegian population or as a category representing lower consumption than the average as described for this age group in Norway (Totland et al., 2010). Details of model parameterization is presented in Table 1 and further as described by Nøst et al. (2013).

2.5. Data treatment and statistical analyses

All statistical analyses were conducted using R, version 3.2.1 (R Foundation for Statistical computing, Vienna, Austria). Statistical significance was defined as $p < 0.05$. All POP results were lipid-adjusted and values below the limit of detection (LOD) were replaced by the LOD divided by √2. One sample result was not available due to technical difficulties. Only max values and the LOD values were presented for compounds with detection frequencies below 40%. Spearman's ρ values were calculated for correlations. We used the Wilcoxon rank sum test (Mann-Whitney *U*-test) to test differences in POP and lipid concentrations between sampling years and sexes.

3. Results

3.1. Characteristics of study participants and POP concentrations across surveys

The proportion of men and women was unequally distributed across the four sampling time points and characteristics of study participants are presented in Table 2. Lipid concentrations were not significantly different among sexes (lowest p-value in Wilcox test 0.057). The fourteen POPs included in the analysis were detected in the majority of samples with the exception of PCB-52, PCB-101 and *p,p′*-DDT for which > 60% of samples were < LOD (detection limits and frequencies

Table 1
Input information to the CoZMoMAN model calculations. Each line represents one model simulation.

Birth year	Sex	No. children	Birth year Child 1	Birth year Child 2	Breast-feeding[a]	Fish consumption
1956	Women	2[b]	1981[c]	1984[c]	6[c]	All combinations specified were run according to two model scenarios for fish consumption[d]:
1964	Women	2[b]	1989[b]	1992[b]	6[b]	1) Average
1971	Women	0[b]				2) Less than average
1977	Women	0[b]				
1956	Men					
1964	Men					
1971	Men					
1977	Men					

[a] Number of months of breast feeding for each child.
[b] Median observation of the women in information obtained in questionnaires.
[c] Assumed similar to the women of the birth year 1964.
[d] Parameterization of fish consumption is described as the average fish consumption in the general Norwegian population in Nøst et al. (2013) and as 'less than average' consumption. 'Average fish consumption' was represented by the scaled consumption rates according to 124 g/day in 2000 and correspondingly for 'less than average consumption' was represented by scaling to 71 g/day in 2000 (Totland et al., 2010). Information on median fish consumption was not available.

Table 2
Descriptive statistics of the randomly chosen 30 year olds in four population surveys in the Tromsø Study. Numbers in parentheses represent numbers of subjects (*N*).

Sampling year		1986	1994	2001	2007
Birth year		1956	1964	1971	1976 (Totland et al., 2010), 1977 (Wolff et al., 2007)
Age		30	30	30	30 (Wolff et al., 2007), 31 (Totland et al., 2010)
Women (*N*)		31	28	24	25
Men (*N*)		14	17	21	20
No. of child births[a]	0	6	8	15	13
	1	10	7	2	4
	2	14	9	6	7
	3	1	4	1	1
Birthyear children		NA[b]	1984–1995	1990–2001	1995–2007
Median birthyear		NA[b]	1988	1994	2000
Median breastfeeding months		NA[b]	6	4	13
Women Cholesterol (mg/dL)	Median	195.7	188.9	186.9	181.8
	Min	141.1	138.8	140.8	73.47
	Max	376.3	261.4	245.6	243.6
Triglycerides (mg/dL)	Median	77.88	85.84	81.42	88.50
	Min	41.59	43.37	38.94	35.40
	Max	319.5	434.5	680.6	309.8
Total lipid (g/L)	Median	4.65	4.78	4.61	4.61
	Min	3.89	3.95	3.68	2.77
	Max	8.74	10.2	13.3	7.68
Men Cholesterol (mg/dL)	Median	224.9	200.7	202.6	175.9
	Min	160.9	114.1	140.0	135.3
	Max	275.3	269.5	244.0	255.2
Triglycerides (mg/dL)	Median	101.3	134.5	131.0	92.92
	Min	53.98	45.13	43.37	53.10
	Max	226.6	365.5	313.3	416.0
Total lipid (g/L)	Median	5.46	5.34	5.33	4.49
	Min	4.00	3.36	3.73	4.04
	Max	7.38	8.52	8.32	9.83

[a] For 1986, 1994 and 2001 there were 2, 4, 14 women, respectively, that did not report any explicit number of children nor any details of any child birth in the questionnaires. These were assumed not to have children.
[b] NA = Not available.

are presented in Table S1). Lipid-normalized POP concentrations are summarized in Table 3 and concentrations in ng/mL serum are provided in Table S2. The POPs detected in highest concentrations were *p,p′*-DDE followed by PCB-153 for both sexes throughout the sampling period (Table 3 and Fig. 1). The median decreases in summed serum POP concentrations (lipid-adjusted) in 1994, 2001, and 2007 relative to 1986 were − 71%, − 81%, and − 86% for women and − 65%, − 77%, and − 87% for men, respectively. The differences between 1986 and 1994 were most significant compared to the other consecutive pairs of sampling years (Table S3). The average annual decreases in medians of summed POP concentrations across the study period were − 4% for both women and men and substantial declines were observed for all compounds (absolute and percentage changes presented in Table S4). Boxplots of concentrations of the two most prevalent POPs, PCB-153 and *p,p′*-DDE, are presented in Fig. 2 for men and women in 1986, 1994, 2001, and 2007.

3.2. Differences between sexes in each sampling year

Concentrations of PCB-153, −156, −170, −180, *oxy*-chlordane and *trans*-nonachlor were higher in men than in women in 1986, 1994 and 2001 (Wilcoxon rank sum test p value < 0.05; Table S5) but differences were not significant across the same years for the other POPs. In 2007, there was no sex difference in any POP concentration with the exception of β-HCH, which was higher among women. When comparing concentrations for men to those for nulliparous women in each sampling year separately, there were fewer compounds with significant differences in all sampling years and in 2001, only β-HCH and *trans*-nonachlor were significant (Table S6). Further, the corresponding comparisons of concentrations in nulliparous and parous women demonstrated that there were significant differences for multiple compounds in several years, especially in 2001 (Table S7), including β-HCH and *trans*-nonachlor that were significantly different between nulliparous women and men in the same sampling year. Concentrations of PCB-153 and *p,p′*-DDE are presented for nulliparous women, parous women and men separately in Fig. S1.

3.3. Intra-POP correlations across sampling years

The correlations between concentrations (lipid-adjusted) for nine of eleven well-detected POPs were high (mostly ≥0.5), but varied across the study period and according to compound (Fig. S2). For many compounds, the correlations were strongest in 1994 or 2007. For example, the correlation of PCB-153 and *p,p′*-DDE was 0.31, 0.70, 0.63, 0.81, and that of PCB-153 and PCB-180 was 0.88, 0.96, 0.94, 0.88 in 1986, 1994, 2001, and 2007, respectively. The two POPs with lowest correlation to any other POP were β-HCH and *p,p′*-DDE.

Table 3
Concentrations (ng/g lipid) of 14 POPs analyzed in serum samples of 30 year olds in four population surveys in the Tromsø Study.

Women	**1986 N = 31**			**1994 N = 28**			**2001 N = 24**			**2007 N = 24**		
	Median	Min	Max	Median	Min	Max	Median	Min	Max	Median	Min	Max
PCB-52	–	< LOD	1990	–	–	< LOD	–	< LOD	300	–	–	< LOD
PCB-101	–	< LOD	1230	–	–	< LOD	–	< LOD	40	–	–	< LOD
PCB-118	31	9	604	9	2	20	9	4	23	5	< LOD	17
PCB-138	101	9	291	40	11	68	21	10	116	18	5	88
PCB-153	165	30	425	65	23	120	43	19	204	30	10	183
PCB-156	14	7	35	4	< LOD	9	4	< LOD	18	3	< LOD	12
PCB-170	35	19	85	14	6	31	9	4	43	7	3	39
PCB-180	94	49	235	46	21	89	25	14	128	19	8	134
HCB	61	28	140	11	4	23	16	9	41	12	5	23
p,p′-DDE	533	28	2340	114	31	295	67	19	1180	46	12	328
p,p′-DDT	23	< LOD	83	–	< LOD	16	–	< LOD	14	–	< LOD	18
β-HCH	25	7	58	4	< LOD	14	5	< LOD	12	3	< LOD	149
oxy-chlordane	9	4	21	3	< LOD	6	3	2	10	2	< LOD	6
trans-nonachlor	15	5	45	7	< LOD	15	7	< LOD	20	4	< LOD	12
Men	**1986 N = 14**			**1994 N = 17**			**2001 N = 21**			**2007 N = 19**		
	Median	Min	Max	Median	Min	Max	Median	Min	Max	Median	Min	Max
PCB-52	–	< LOD	84	–	–	< LOD	–	–	< LOD	–	–	< LOD
PCB-101	–	< LOD	11	–	–	< LOD	–	< LOD	22	–	–	< LOD
PCB-118	31	15	62	16	7	27	9	6	28	4	2	11
PCB-138	121	68	200	52	30	209	35	20	102	18	8	35
PCB-153	218	119	338	99	61	348	60	38	171	35	19	66
PCB-156	24	16	37	8	5	26	6	2	12	2	< LOD	7
PCB-170	58	32	79	23	16	68	13	9	31	9	4	18
PCB-180	164	95	226	71	46	226	39	24	98	24	13	50
HCB	78	50	152	16	9	33	19	8	46	11	5	18
p,p′-DDE	438	106	718	110	57	366	73	32	1650	39	16	79
p,p′-DDT	19	< LOD	53	–	< LOD	19	–	< LOD	14	–	–	< LOD
β-HCH	20	14	53	4	< LOD	8	4	< LOD	32	–	< LOD	5
oxy-chlordane	15	6	23	6	2	23	5	2	13	2	< LOD	5
trans-nonachlor	38	11	62	12	4	66	12	5	23	6	< LOD	14

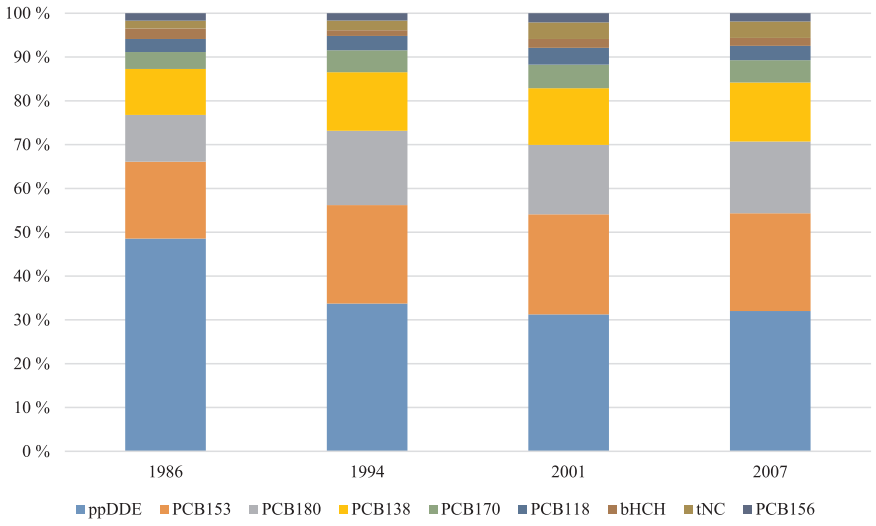

Fig. 1. Relative contributions of individual POPs to their sum (in %) in serum samples from four sampling years (men and women combined). The figure is based on the most prevalent POPs in lipid weight concentrations as presented in Table 3.

3.4. Predictions of PCB concentrations

Predicted concentrations (ng/g lipid) of PCB-153 were within a factor of 1.33, 2.57, 3.60, 3.00 of the median concentrations measured in 1986, 1994, 2001, 2007, respectively, in women and 1.12, 2.10, 2.12, 2.55 in men, if assuming fish consumption in the persons corresponding to the average in the Norwegian population (Fig. 3 and Table S8). When assuming less than Norwegian average fish consumption, the predicted concentrations were within a factor of 0.76, 1.85, 2.33, 2.40 of those measured in the same sampling years in women and 0.67, 1.39, 1.55, 1.76 in men, respectively. The decreases in concentrations in PCB-153 in 1994, 2001, and 2007 compared to 1986 were −60%, −74%, −82% for median measurements in women and the corresponding numbers decreases were −4%, −20%, −43% for the predicted concentrations. For men, the observed decreases were −55%, −72%, −84%, and the predicted decreases were -6%, −36%, and −58% in the respective years.

3.5. Comparing biomonitoring results in the Tromsø Study

Median concentrations of PCB-153 (ng/g lipid) in the 30 year old men were 61%, 39%, 25%, and 20% in 1986, 1994, 2001, and 2007 of

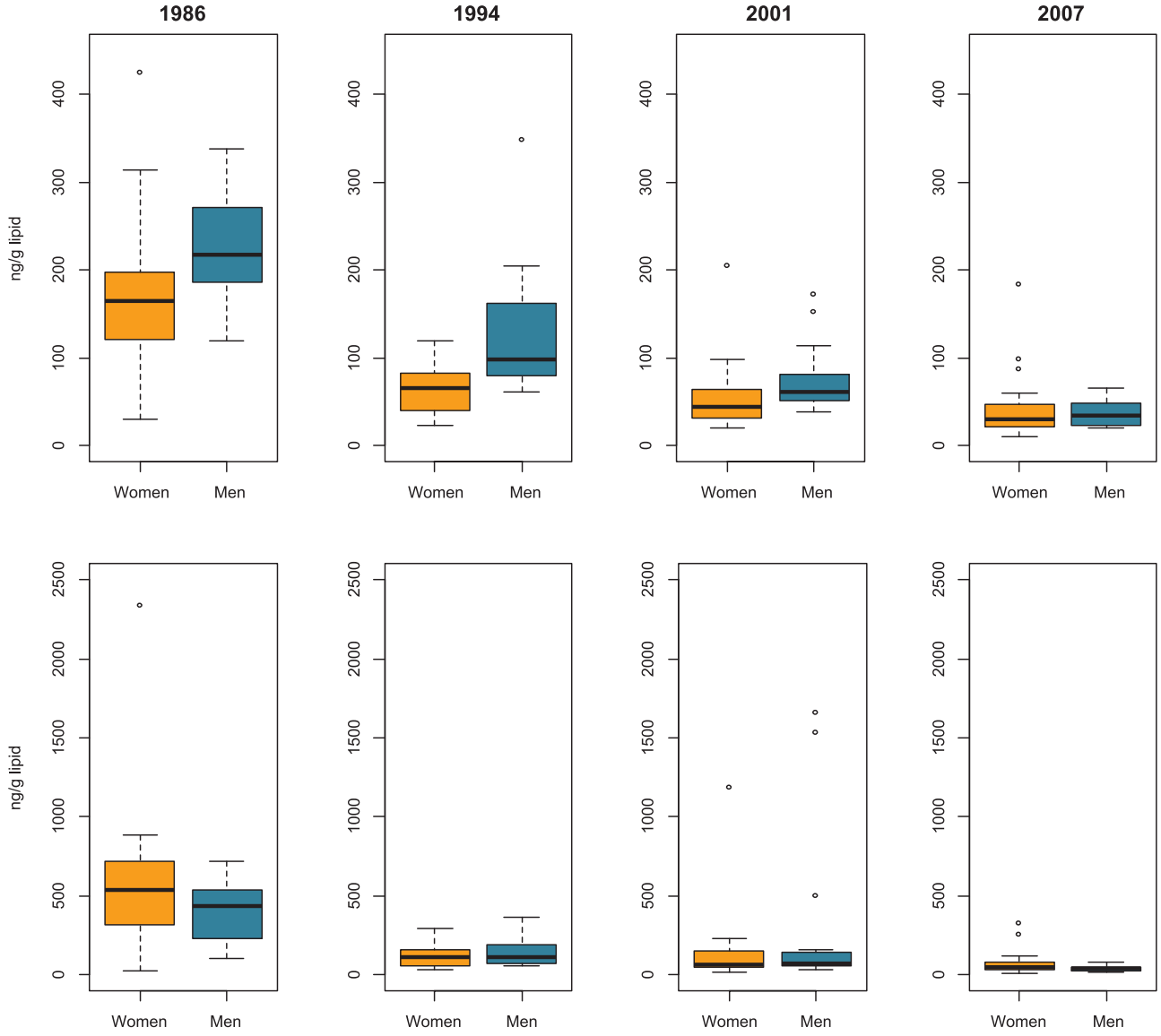

Fig. 2. Serum concentrations of PCB-153 (upper) and *p,p′*-DDE (lower) in ng/g lipid weight for 30 year old women and men in Northern Norway in the sampling years 1986, 1994, 2001, and 2007. Boxes represent the 25th–75th percentiles, horizontal lines represent the median, whiskers indicate 1.5 times the length of the interquartile range above and below the 75th and 25th percentiles, respectively, and outliers are represented as data points.

those in the longitudinal study of older men in the same sampling years in the Tromsø Study (Fig. 4). Further, the observed relative decreases in the 30 year old men were −55%, −72%, −84% for 1994, 2001, and 2007 relative to 1986 and the corresponding decreases for the same sampling years in the older Tromsø men were −31%, −33% and −53%, respectively. Concentrations in men in this study were very similar to corresponding results from a previous study including repeated cross-sectional samples of pooled blood from Norwegian men in the age group 40–50 years old (Thomsen et al., 2007). No comparable study was found that included only women and thus women are not displayed in Fig. 4. However, the time trend in women in this study was similar to the trend in men.

4. Discussion

4.1. Changes in POP concentrations in the 30 year olds from 1986 to 2007

This study of serum POP concentrations in repeated cross-sections of 30 year old men and women from Northern Norway adds to the evidence of decreasing environmental and human concentrations of many legacy POPs in many countries during the study period. All compounds demonstrated decreasing concentrations across sampling years and the largest decrease was observed from the first survey in 1986, especially for HCB and β-HCH. Time trends such as those observed in this study are compelling results of decreasing concentrations in human exposure media following strengthened regulation of production and use of these compounds since the 1970s (Nøst et al., 2017; Bignert et al., 1998; Hung et al., 2010; Rigét et al., 2010). Our observations could reflect that the decreases in emissions of POPs studied were possibly largest early in the sampling period and that the relative decreases differed across compounds according to differences in emission histories as well as in environmental and human degradation/elimination rates (Nøst et al., 2017).

As calculated across the study period, the annual decreases in concentrations of all PCBs in the 30 year olds were −4% for both women and men across the study period and the yearly percentage changes across the study period were very similar across compounds (Table S4). The observed decline in this period is steeper compared to observations for PCBs in pooled blood samples from Norway with overlapping sampling years (-2.9% during 1977–2003) and less pronounced than an

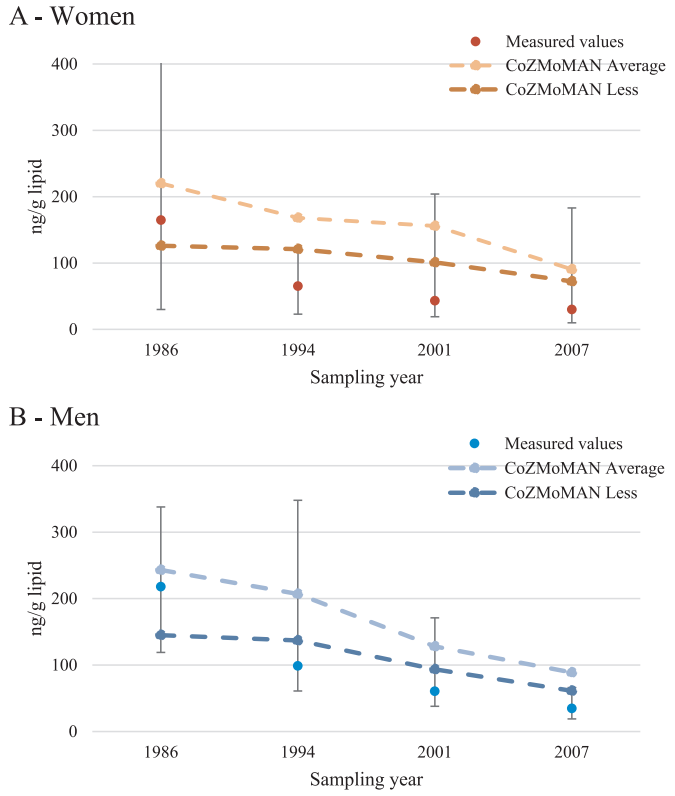

Fig. 3. Comparing measured concentrations of PCB-153 (ng/g lipid; dots represent median and whiskers the lowest and highest measurements) in the four sampling years to predictions (dashed lines) obtained from the time-variant CoZMoMAN model. Predictions were obtained based on median descriptive information from the study participants as described in Table 1 with separate lines representing predictions for average fish consumption in the Norwegian population and one category of less than average consumption.

observed decline for PCBs in blood in Sweden (-7.2% during 1993–2007) (Hardell et al., 2010). Although study periods did not completely overlap, the periodic changes in concentrations between studies were of the same magnitude. Overall, rates of declines for the exposures in these study groups in Norway and Sweden were rather similar and these observations are in accordance with extensive monitoring results demonstrating decreasing concentrations of many legacy POPs in the environment (Bignert et al., 1998; Hung et al., 2010; Rigét et al., 2010) and in humans (Hovinga et al., 1992; Høyer et al., 2000; Tee et al., 2003; Vo et al., 2008; Nøst et al., 2013, 2017; Hardell et al., 2010) in many countries in the same time period.

Concentrations in the 30 year old women in 2007 were similar to those in women in Northern Norway in 2007–2008 during and after their pregnancy (Hansen et al., 2010). Concentrations in the 30 year old men were similar to those observed in pooled samples of 40–50 year old men in Norway during 1977–2003 (Thomsen et al., 2007).

The age group of 30 year olds was chosen to obtain relevant biomonitoring results that could reflect exposure for reproductively active ages in the source population. This is relevant with regards to translating knowledge of changing human exposure into conjectures of prenatal exposure for the young and future generations. This study has shown that exposures to legacy POPs for men and women at reproductive ages in Northern Norway has decreased considerably since the 1980s. If assuming similar breast-feeding behaviors among women throughout the same period, early life exposures to the same compounds in the Norwegian population have also been extensively reduced during the last decades.

4.2. Comparing biomonitoring results from different study designs

The concentrations of POPs in the 30 year olds were lower in each sampling year compared to observed concentrations in our previous longitudinal study of older men from the same population surveys (in that study, median age increased from 50 to 71 between 1986 and 2007 and ranged 36–61 in 1986). This was expected as cross-sectional biomonitoring studies have frequently observed positive associations between concentrations of many POPs and age (e.g. Hardell et al., 2010; Wolff et al., 2005) due to higher historic exposure in the older birth cohorts (Quinn and Wania, 2012). Also, the current study group included women that had slightly lower concentrations of POPs which is likely due to the loss processes related to child birth and breast feeding (e.g. Hardell et al., 2010; Wolff et al., 2007).

In the present study, the age group was fixed across sampling times whereas the birth cohorts varied. This study design differed from our previous longitudinal study using repeated individual measurements (where birth cohort was fixed and age varied across sampling years) and provides important information about age-period-cohort effects of POPs. The inter-individual time trends in 30 year olds in the current study were more pronounced as compared to the intra-individual time trends observed in older men in the same geographical region. The steeper decline in the 30 year olds could reflect birth cohort effects

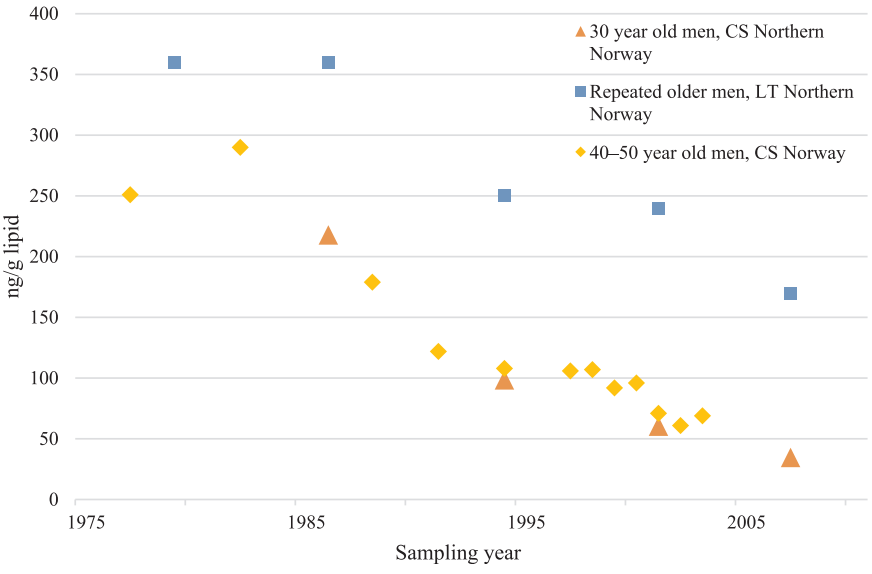

Fig. 4. Comparing the concentrations of PCB-153 (ng/g lipid) in the two Norwegian repeated cross-sectional (CS) sampling of 30 year old men (present study) or 40–50 year old men (Thomsen et al., 2007) and the longitudinal (LT) study including repeated individual measurements in older men (median age increased from 43 to 71 between 1979 and 2007 and ranged 29–54 in 1979) (Nøst et al., 2013).

related to a relative higher historic exposure in the older age group (previous longitudinal study). Further, continued exposure to POPs after decreased environmental emission could also be higher in the older men compared to the younger study groups related to behavioral differences, e.g. higher fish consumption in the older group. These comparisons demonstrated variation in time trends observed within the same population in the exact same sampling years, which is explained by differences in study design (selected age group and whether time trends between individuals or within individuals were assessed). Nevertheless, both studies provide evidence of declining POP concentrations.

Using the design of repeated sampling of a set age group was also performed in a previous Norwegian study (Thomsen et al., 2007). The study included pooled blood samples of men in the age group 40–50 years old and the observed concentrations and time trends in that study were very similar to that in the 30 year olds in Northern Norway (Fig. 4). Thus, the time trends demonstrated in the three studies targeting time trends using different designs were in overall agreement and the biomonitoring efforts in these study periods revealed similarly declining concentrations in adults in Norway. Still, birth cohort effects were evident and the interpretation of biomonitoring studies must regard historic exposures and birth cohort effects (Nøst et al., 2017; Quinn and Wania, 2012; Ritter et al., 2009).

4.3. Evaluation of time-variant model estimations

Evaluation of model predictions of human POP concentrations using comparisons with measurements are important to challenge model parameterizations of historic emissions and environmental and human fate to eventually increase credibility in mechanistic models. Models such as CoZMoMAN can help to increase the mechanistic understanding of relationships between emissions and environmental and human fate processes that are hard to deduct from observations alone.

Overall, the slopes in decreasing time trends for PCB-153 estimated by the CoZMoMAN model (4 time points) were in reasonable agreement with the observed concentrations (all within factor 3). Median concentrations were over-predicted in the last three sampling years and imply that the model predictions for human exposure media (e.g. estimated dietary consumption) was overestimated. Median concentrations were chosen for the observations as most input to the model (not dietary information) was based on median information from the study group although mean concentrations measured agreed slightly better (results not presented). Still, the predicted relative declines were in overall agreement with those measured, especially in men, and also in agreement with declines in predicted PCB concentrations in older men in our previous longitudinal study (Nøst et al., 2013). Of note, a modest predicted decrease from 1986 to 1994 was also observed in that study. A smaller range for the parameterized women and men was predicted for the recent years compared to the earlier years and was likely resulting from more homogenous parameterization of the environmental exposures and no child births.

Agreement of absolute concentrations was better for 30 year old men and women when assuming less fish consumed compared to the Norwegian average. Indeed, lower than average fish consumption is expected for this age group in Northern Norway and it is lower compared to older age groups (Totland et al., 2010). Thus, it represented the more realistic scenario of the two regarded, especially for recent years. Any temporal trend in dietary intakes (e.g. cohort dependent changes in fish intakes) was not regarded by the model and thus cannot be disregarded as a source of discrepancy between measured and predicted concentrations. The better agreement observed for older men (Nøst et al., 2013) could be due to that they were relatively more exposed from fish consumption and that the main exposure pathway, represented by fish intake, is better characterized for this study group as compared to the younger 30 year olds. The predictions were in better agreement with observations for men as compared to women and likely reflected the variation introduced when regarding model parameterization of child births and related loss processes.

The overall observation is that the concentration trends observed in human biomonitoring are in accordance with predictions from mechanistic modeling as this study was within a factor 3 of measurements. CoZMoMAN predictions for PCB concentrations (Breivik et al., 2010; Quinn and Wania, 2012; Nøst et al., 2016) and their temporal changes (Nøst et al., 2013) have previously demonstrated acceptable performance within the ranges of measured concentrations, especially on group basis as performed in this study. Predictions in individual humans have also been evaluated against single blood sample measurements (Nøst et al., 2016; Wood et al., 2016; Rylander et al., 2015) and have shown similar agreement (most predictions within factor 3) as in this study using group comparisons. Collectively, such studies confirm the relations between past emissions of POPs and the exposures experienced by humans (Nøst et al., 2013, 2017; Quinn and Wania, 2012; Ritter et al., 2009).

4.4. Differences in POP concentrations between sexes

Median concentrations of POPs were higher among men in the first three sampling surveys but no difference among sexes was evident in 2007, although concentrations were slightly higher for β-HCH in women. Higher concentrations in men have been observed in other populations in overlapping study periods and have been largely ascribed to differences in body lipid distributions between sexes and excretion of POPs related to childbirth, especially through breast-feeding, in women (e.g. Hardell et al., 2010; Wolff et al., 2007). There were few nulliparous women among the women included in the first two study years but more in the last sampling years. Thus, it is likely that a fraction of the difference between sexes in the early sampling years were augmented due to lowered concentrations in parous women due to loss related to child birth. Indeed, the sex differences were not as significant across men and nulliparous women in each year and there were differences across nulliparous women and parous women, although depended on sampling year and the number of women in each year was small. Thus, differences between men and women and between parity groups varied across sampling years and likely reflected sex differences in exposures and degradation rates and the relative importance of loss of PCB-153 through birth and breast-feeding according to the trends in environmental exposures (Nøst et al., 2016). Notably, the observed sex differences for concentrations of PCB-153 were reproduced in the model predictions and likely reflects that model parameterizations adequately captures gender differences in exposure and overall loss processes.

4.5. Temporal variation in POP composition

Concentrations of *p,p′*-DDE contributed the most to the summed POP concentrations in all years but the relative contribution of this compound to the summed POP concentrations decreased. PCB congeners 153, 180, 138 dominated summed PCB concentrations in the latest three sampling years. The changes in relative composition of compounds can likely be explained by concurrent processes reflecting decreased emissions as well as environmental degradation and human elimination half-lives that both have compound-specific rates. For example, the large decreases for *p,p′*-DDT, β-HCH and HCB between the first two consecutive sampling years likely reflect less exposure to and excretion of POPs with shorter half-lives (Woodruff et al., 1994), rendering POPs with longer apparent half-lives, e.g. the higher chlorinated PCBs (Shirai and Kissel, 1996), with higher relative importance in the more recent sampling years. Further, control strategies are more efficient at reducing primary emissions of pesticides as compared to PCBs due to the long half-lives of products containing PCBs (Breivik et al., 2007) and secondary emissions which also likely influenced the trends observed across different POPs.

Correlations between POPs were moderate or strong for most compounds in all sampling years but no evident trend could be interpreted from POP correlations across sampling years. Small differences in correlations might reflect compound-specific transitions in dominating influence of recent primary emissions to the environment and recent exposures versus dominating influence of environmental and human persistence of POPs of past exposures. Still, their consistent strong correlations implicate similar rates of observed decreases that again suggest similar declines in trends in production and use (Breivik et al., 2007; Schenker et al., 2008; Li et al., 2005) as well as environmental and human persistence. Accordingly, dietary patterns have been associated with blood concentrations of POPs in pregnant women in Northern Norway (Veyhe et al., 2015) and demonstrate the importance of this exposure route to women in age ranges that include the 30 year olds in this study. However, certain POPs, especially β-HCH, were weakly correlated to the other measured POPs and suggest less similar rates of concentration declines and/or exposure pathways for certain POPs.

4.6. Study strengths and limitations

As this study consisted of a limited sample number and included both men and women (both nulliparous and parous women), a thorough evaluation of all predictive factors could not be performed by statistical analyses. Especially, the low number of subjects hampered the assessment of parity among women in each year. Also, individual dietary information was not available for the model parameterization and we used estimates of average consumption in Norwegian populations to reflect the fish consumption in the study population (Nøst et al., 2013). Further, breast-feeding information was not available for all women in the first sampling year so we used the median estimates for the two subsequent sampling years (they were the same). Still, these assumptions are likely valid.

Sample integrity was considered good based on the results from our past study where we evaluated the sample integrity by reanalyzing lipid concentrations. We found very little discrepancy between lipid concentrations from the time of blood sampling and those of a reanalysis for most samples at time of analyses in 2012 (Nøst et al., 2013).

Comparisons between the biomonitoring results in the 30 year olds and those of the previous study including older men could be somewhat confounded by laboratory differences as results originated from two different laboratories. Still, both studies have meet the QA-QC criteria for the sample preparations and the laboratories both perform well in the interlaboratory study in the Arctic Monitoring and Assessment Programme ring test system (organized by the Centre de toxicologie du Québec of the Institut national de santé publique du Québec (2013)).

Future monitoring studies should include more recent samples and expand the selection of compounds to include both established POPs as well as other compounds of increasing concern where human exposure has been recent or current.

4.7. Summary of key findings

Declines in serum concentrations from 1986 to 2007 were substantial for legacy POPs in men and women at reproductive ages in Northern Norway and are generally consistent with previous longitudinal biomonitoring results in the study population. Especially, men and women of reproductive age had lower concentrations and more pronounced declines compared to older and aging men. The measured concentrations and observed declines likely reflect a combination of recent and historic exposures. The small differences in trends observed could thus be attributed to different study designs, i.e. the age group, gender and cross-sectional vs longitudinal design.

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Declarations of interest

None.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.envres.2019.02.047.

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