Monitoring of POPs in human milk from Stockholm and Gothenburg, 1972-2015

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Övervakning av POPs i bröstmjölk från Stockholm och Göteborg, 1972-2015

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1 Introduction

This report summarises the monitoring activities regarding POPs in human milk from Stockholm and Gothenburg within the National Swedish Monitoring Programme for Human Health. It is the result of joint efforts from the *Mothers´ Milk Center* at Stockholm South General Hospital (collection of samples in Stockholm); the *Department of Occupational and Environmental Medicine* at Sahlgrenska University Hospital (collection of samples in Gothenburg); the *Department of Environmental Science and Analytical Chemistry* at Stockholm University (analyses of organochlorines, flame retardants and perfluorinated compounds); the *Swedish National Food Agency* (analyses of dioxins); and the *Department of Environmental Research and Monitoring* at the Swedish Museum of Natural History (SMNH) (co-ordination, administration and preparation, freeze-storage of human milk in the Environmental Specimen Bank (ESB) for retrospective studies, data preparation and statistical analyses). The monitoring programme is financed by the *Swedish Environmental Protection Agency* (SEPA).

The objectives can be summarised as follows:

- to estimate the levels of organochlorines (PCBs, DDTs, HCHs and HCB), brominated flame retardants (PBDEs, HBCDD and DBE-DBCHs), perfluorinated substances (PFASs) and dioxins (PCDDs, PCDFs and dl-PCBs) in human milk from Stockholm and Gothenburg, and to compare concentration both on a national and international scale.

- to monitor long term time trends in Stockholm (1972-2014) and Gothenburg (2007-2015) and to estimate the rate of changes found in comparison to time trends reported in milk from Uppsala;

- to investigate large scale spatial differences in substance pattern between Stockholm and Gothenburg.

- to investigate if the individual variation in PFASs differ between Stockholm and Gothenburg

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2 Utökad svensk sammanfattning

Dr. Koidu Norén, vid Karolinska Institutet, initierade övervakning av human hälsa i Sverige när hon började samla in och analysera organiska föroreningar i modersmjölk från Stockholmsområdet redan 1967. Sedan 1972 har de prover som samlats in lagrats frusna för retrospektiv analys av miljöföroreningar. År 1997 överfördes denna mjölksamling till miljöprovbanken vid Naturhistoriska Riksmuseet i Stockholm som då även tog över ansvaret för insamlingen i Stockholmsområdet, via Modersmjölkcentralen på Södersjukhuset. Modersmjölk har även samlats in i Göteborg sedan 2007 via Modersmjölkcentralen/Arbets- och miljömedicinska institutionen på Sahlgrenska Universitetssjukhuset.

I denna rapport sammanfattas den nationella övervakning av modersmjölk med avseende på persistenta organiska miljögifter, som utförts sedan 1972 från Stockholm och Göteborg och som finansierats av Naturvårdsverket.

Syftet med studien kan sammanfattas enligt följande:

• Undersöka halter av klorerade ämnen (PCBer, DDTer, HCHer, HCB, dioxiner och furaner), bromerade flamskyddsmedel (PBDEer, HBCDD och DBE-DBCH) samt perfluorerade ämnen (PFASs) i modersmjölk från Stockholm och Göteborg.

• Utvärdera långsiktiga tidstrender i Stockholm (1972-2014) och Göteborg (2007-2015).

• Undersöka skillnader i mönster av samansättningen av de övervakade ämnena mellan Stockholm och Göteborg.

• Undersöka om variationen på individnivå gällande PFASs skiljer sig mellan Stockholm och Göteborg 2012.

Fetthalt
Modersmjölk från Stockholm uppvisade generellt en uppåtgående trend i fetthalt under hela övervakningsperioden (1972-2014), även om en nedåtgående trend observerades under den senaste tioårsperioden. En förändring av analysmetod 2011 kan emellertid ha påverkat utvecklingen under den senaste tioårsperioden. En ökning i fetthalt indikerades i modersmjölk från Göteborg (2007-2015). Fetthalten var något högre i modersmjölk från Göteborg 2015 jämfört med modermjölk från Stockholm 2014 (4.0 respektive 3.4 %). Fetthalter som rapporterats i andra studier är ligger i nivå med de fetthalter som rapporterats i denna studie.

PCBer
Halterna av samtliga kongener som uppmätts, d.v.s. CB-180, CB-153, CB-138 och CB-118 minskade över tid (7-11 % per år) i modersmjölk från både Stockholm och Göteborg, med undantag för CB-28 för vilken ingen trend kunde detekteras. De minskande halterna över tid stämmer väl överens med temporala trender som rapporterats i modersmjölk från Uppsala (7 % per år) (1996-2012) samt i japansk modersmjölk (7.5 % per år). Koncentrationerna av de uppmätta kongenerna var jämförbara mellan Stockholm och Göteborg och låg även på liknande nivåer som i modersmjölk från Uppsala. I jämförelse med andra europeiska länder var koncentrationerna av CB-153 (som är den kongenern som generellt sett förekommer i

högst halter i modersmjölk) lägre än i övriga Europa. Inga signifikanta skillnader detekterades gällande PCB-kongenermönster mellan Stockholm och Göteborg.

DDTer, HCHer och HCB
Koncentrationerna av DDE, DDT och HCB i modersmjölk från Stockholm (1972-2014) minskade över hela övervakningsperioden (7-11 % per år) vilket även halterna av DDE och DDT i modersmjölk från Göteborg (2007-2015) gjort under den senaste tioårsperioden (7 och 12 % per år). Tidstrender för DDE i modersmjölk från Uppsala (1996-2012) och Japan uppvisar minskande halter i samma storleksordning (7.4 och 9.1 % per år). Även halterna av HCB i modersmjölk från Uppsala minskar (5.9 % per år). Koncentrationerna av DDE, DDT samt β-HCH var något högre i Stockholm än i Göteborg, medan HCB halterna var något högre i modersmjölk från Göteborg. Koncentrationerna av DDE, HCB och β-HCH låg i nivå med koncentrationer uppmätta i modersmjölk från Uppsala, men låg i det lägre spannet av koncentrationer rapporterade från andra europeiska länder. Ingen signifikant skillnad i mönster observerades för DDE-, DDT-, HCB- och β-HCH i modersmjölk mellan Stockholm och Göteborg.

PCDDer/PCDFer och dl-PCBer
Koncentrationerna av ΣPCDDer, ΣPCDFer, Σdl-PCBer och ΣPCDDer + PCDFer + dl-PCBer i modersmjölk från Stockholm (1972-2014) och Göteborg (2007-2015) minskade sett över hela övervakningsperioden (5.6-6.5 % per år). Under den senaste tioårsperioden har dock inga signifikanta minskningar observerats i modersmjölk från Stockholm. En tänkbar förklaring till detta skulle kunna vara att det skett ett byte i analyslaboratorium 2012 vilket kan ha påverkat möjligheten att upptäcka trender. Halterna i modersmjölk från Uppsala (1996-2012) minskade i samma storleksordning som i Stockholm och Göteborg sett över hela tidsperioden. Koncentrationerna av ΣPCDDer, ΣPCDFer, Σdl-PCBer och ΣPCDDer + PCDFer + dl-PCBer var jämförbara mellan Stockholm och Göteborg och även jämförbara med koncentrationer uppmätta i modersmjölk från Uppsala. I jämförelse med andra europeiska länder låg de i det lägre spannet. Ingen signifikant skillnad i mönster observerades för ΣPCDDer, ΣPCDFer, Σdl-PCBer mellan Stockholm och Göteborg.

PBDEer och HBCDD
Koncentrationerna av BDE-47, BDE-99 och BDE-100 i modersmjölk från Göteborg minskade 2007-2015 (18-21 % per år). I kontrast till detta observerades inga signifikanta log-linjära tidstrender i modersmjölk från Stockholm, varken över hela tidsperioden eller under den senaste tioårsperioden. Dock var koncentrationerna av BDE-47, BDE-99 och BDE-100 i de två proven från 2013 (Stockholm) avsevärt högre än koncentrationerna omkringliggande år vilket påverkar möjligheten att upptäcka trender under den senaste tioårsperioden. Bytet av analyslaboratorium 2010 kan också ha påverkat möjligheten att detektera trender. Den minskning av BDE koncentrationer som rapporterats i modersmjölk från Göteborg i denna studie är i samma storleksordning som den förändring som rapporterats i modersmjölk från Uppsala (1996-2012) (5-10 % per år). Koncentrationerna av samtliga bromerade flamskyddsmedel rapporterade här (d.v.s. BDE-28, BDE-47, BDE-99, BDE-100, BDE-153 och HBCDD) var högre i Stockholm än i Göteborg. Koncentrationer uppmätta i modersmjölk från Uppsala var högre än i Göteborg men lägre än i Stockholm, med undantag för HBCDD där halterna i Uppsalamjölken även var högre än i Stockholmsmjölken. I jämförelse med andra europeiska länder låg halterna av BDE-47 i Stockholmsmjölken i jämförbar nivå, medan HBCDD halterna i modersmjölk från både Stockholm och Göteborg låg lägre. Det fanns ingen signifikant skillnad i mönstret för BDE-47, BDE-99, BDE-100, BDE-153 och HBCDD mellan Stockholm och Göteborg.

PFAS

Koncentrationerna av PFDA, PFHxS, PFNA, PFTriDA och PFUDA i modersmjölk från Stockholm ökade signifikant under hela övervakningsperioden (1972-2014), medan PFOA-koncentrationerna minskade. Koncentrationen av PFNA och PFDA ökade även i blodprover från ammande kvinnor i Uppsala (1996-2010). I modersmjölk från Göteborg upptäcktes signifikanta nedåtgående trender (2007-2015) för PFDoDA, PFHxS och PFOA, och det var även fallet för PFOS i Stockholm under den senaste tioårsperioden. Inga generella skillnader i koncentration observerades mellan Stockholm and Göteborg. I jämförelse med modersmjölk från andra länder över hela världen var halterna av PFOS och PFOA jämförbara, men i det lägre spannet, vilket även var fallet i jämförelse med koncentrationer i modersmjölk från Uppsala (2004). Ingen signifikant skillnad i mönster observerades för PFOA, PFOS, PFNA, PFDA, PFUDA och PFTriDA mellan Stockholm och Göteborg. Den individuella variationen 2012 var störst för PFTeDA i modersmjölk från både Stockholm och Göteborg. PFOA, PFUA och PFNA uppvisade den lägsta individuella variationen. FOSA uppvisade en signifikant skillnad i individuell variation mellan modersmjölk från Stockholm och Göteborg, vilket skulle kunna indikera en skillnad i kontaminering. Dock uppmättes det ingen signifikant skillnad för kvarvarande PFAS.

3 Summary

The environmental contaminants examined in this report can be classified into five groups – organochlorine pesticides (DDTs, HCHs and HCB), polychlorinated biphenyls (PCBs), brominated flame retardants (PBDEs and HBCDD), dioxins, furans and dioxin-like PCBs (PCDD/PCDFs and dl-PCBs) and perfluorinated compounds (PFASs). Each of these contaminants has been examined in human milk from Stockholm and Gothenburg. The following summary examines overall trends, both spatial and temporal, for the five groups and also individual differences in PFASs concentration between Stockholm and Gothenburg.

Fat Content
Human milk from Stockholm displayed an upward trend in fat content during the whole monitoring period, although a downward trend was observed during the most recent ten years. However, a change in analythical method in 2011 might have had an impact on the trend during the most recent ten years. Increasing fat content was indicated in human milk from Gothenburg (2007-2015). The fat content estimated from the smoothed line was slightly higher in the milk from Gothenburg than in the milk from Stockholm.

PCBs
Generally, a downward trend was observed for all congeners measured i.e. CB-180, CB-153, CB-138 and CB-118 in human milk from both Stockholm and Gothenburg, with the exception of CB-28 for which no trend was detected. The concentrations of the measured congeners were comparable between Stockholm and Gothenburg and there was no significant difference in PCB congener pattern between the two cities.

DDTs, HCHs and HCB
The concentrations of DDE, DDT and HCB in human milk from Stockholm decreased significantly during the whole monitoring period and so did DDE and DDT in the milk from Gothenburg during the most recent ten years. The concentrations of DDE, DDT and β-HCH estimated from the smoothed line were slightly higher in Stockholm than in Gothenburg whereas HCB was slightly higher in Gothenburg. There was no significant difference in the DDE, DDT, HCB and β-HCH pattern between Stockholm and Gothenburg.

PCDD/PCDFs and dl-PCBs
The concentrations of ∑PCDDs, ∑PCDFs, ∑dl-PCBs and ∑PCDDs+PCDFs+dl-PCBs in human milk from Stockholm and Gothenburg decreased significantly during the whole monitoring period. However during the most recent ten years no trends were observed for the Stockholm milk. The concentrations were comparable between Stockholm and Gothenburg and there was no significant difference in the pattern for ∑PCDDs, ∑PCDFs, ∑dl-PCBs between Stockholm and Gothenburg.

PBDEs and HBCDD
The concentrations of BDE-47, BDE-99 and BDE-100 in human milk from Gothenburg decreased significantly during 2007-2015 whereas no trends were observed in the milk from Stockholm. The concentrations estimated from the smoothed line were higher in Stockholm than in Gothenburg for all BFRs reported here (i.e. BDE-28, BDE-47, BDE-99, BDE-100, BDE-153 and HBCDD). There was no significant difference in the pattern for BDE-47, BDE-99, BDE-100, BDE-153 and HBCDD between Stockholm and Gothenburg.

PFASs

The concentrations of PFDA, PFHxS, PFNA, PFTriDA and PFUDA in human milk from Stockholm increased significantly during the whole monitoring period, whereas PFOA concentrations were decreasing. In the human milk samples from Gothenburg significant downward trends were detected for PFDoDA, PFHxS and PFOA and that was also the case for PFOS in Stockholm for the most recent ten years. There were no general differences in the concentrations estimated from the smoothed line between Stockholm and Gothenburg and no significant difference in the pattern was observed for PFOA, PFOS, PFNA, PFDA, PFUDA and PFTriDA between Stockholm and Gothenburg.

4 Sampling

4.1 Sample collection

To reduce influence of confounding factors, which in turn reduces the variation between the samples, the sample definition is narrow and restrictive. The selected mothers were all healthy and non-smokers. They were predominantly primiparous (having their first baby) because studies have shown a correlation between contaminant level and the number of children a woman has given birth to (Dillon et al. 1981, Albers et al. 1996, Fitzgerald et al. 2001). Women of similar age were sampled because as age of the mother increases, levels of POPs in the fat generally also increase (Albers et al. 1996). Samples were collected from 2 weeks up to three months after delivery to minimize variation in the milk composition, which apart from water mainly consists of carbohydrates, proteins and fat. The composition of human milk changes considerably over time post-partum and fat content is the most variable component (Mitoulas et al. 2002).The mothers were born and have resided in Sweden for their entire lives to ensure that the contaminant level in the milk was representative of a Swedish contaminant load.

4.1.1 Stockholm

Dr. Koidu Norén, at Karolinska Institute, Sweden, initiated human health monitoring in Sweden when she began collecting and analysing organic contaminants in mothers' milk from the Stockholm area in 1967 (Norén and Meironyté 2000). The milk was supplied by the Mothers' Milk Centre in Stockholm (Meironyte et al. 1999), which has continued to supply milk for contaminant monitoring up until today. Dr Norén and her research group have analysed a wide range of persistent organic contaminants and their metabolites in human milk samples (Norén and Meironyté 2000, Meironyte et al. 1999, Norén et al. 1996, Norén and Lundén 1991). The samples, collected since 1972, were stored frozen for future re-analysis. In 1997, this milk collection was transferred to the ESB at SMNH. In general 100-200 individual samples per collected year (1972, 1974, 1976-80, 1984, 1988-92, 1994-98) are stored in pools of 20-100 individuals per pool or in some cases as individual samples.

The collection of human milk in Stockholm, 1999-2007, was administrated by Maria Athanasiadou at the Department of Environmental Chemistry at Stockholm University. From 2008 and onward the collection was administrated by the Department of Environmental Research and Monitoring at the SMNH. In general 20 individual samples per year were stored for analysis.

4.1.2 Gothenburg

Human milk has been collected in Gothenburg since 2007. The milk was initially collected at the Mothers´ Milk Centre at Sahlgrenska University Hospital, and the milk with too high bacterial content was later on transferred to the Department of Occupational and Environmental Medicine at Sahlgrenska University Hospital. In general, 10-20 individual samples per year were stored for analysis.

4.2 Sample preparation and registered variables

The samples were initially stored at -20ºC in plastic bags and plastic bottles at the Mothers' Milk Centre at Stockholm South General Hospital in Stockholm and at the Department of Occupational and Environmental Medicine at Sahlgrenska University Hospital and Academy in Gothenburg. After transfer to the ESB, the samples were thawn and stored both as individual samples and in pools (about 10 individuals in each pool) all in pre-washed glass bottles with lids covered with aluminium foil stored at -20ºC.

A record of these specimens including; information on age and parity, notes about available amounts, together with a precise location in the cold-store are kept and accessible through a database.

Table 4.1 Sampling site and year of sampling, N=number of donating mothers and which samples that has been analysed for perfluorinated substances (PFASs), brominated flame retardants (BFRs), dioxins and organochlorines (ClCs). All samples are from the Environmental Specimenbank at the Swedish Museum of Natural History in Stockholm.

Samplingsite Year	N	Mean age (years)	Primaparous (%)	PFASs	BFRs	Dioxins	ClCs
Stockholm							
1972	75[a]	27-28	NA[b]	YES			
1976	78[a]	27-28	NA[b]	YES			
1980	116[a]	27-28	NA[b]	YES			
1984/85	102[a]	27-28	60	YES			
1988	20[a]	30	65	YES			
1992	20[a]	29	65	YES			
1996	20[a]	31	75	YES			
2000	20[a]	30	75	YES			
2004	20[a]	30	80	YES			
2008	18[a]	28	100	YES			
2009	10[a];10[a]	31	100	YES			
2010	10[a];9[a]	30[c]	100	YES	YES		YES
2011	11[a];11[a]	30	100	YES	YES		YES
2012	20[d];10[a]; 11[a]	31	100	YES	YES	YES	YES
2013	10[a];10[a]	26	100	YES	YES	YES	YES
2014	10[a];11[a]	30	100	YES	YES	YES	YES
Gothenburg							
2007	5[a];5[a]	30	100	YES		YES	
2008	8[a];8[a]	NA[b]	NA[b]	YES		YES	

Samplingsite Year	N	Mean age (years)	Primaparous (%)	PFASs	BFRs	Dioxins	ClCs
2009	8[a]	29	75	YES		YES	
2010	11[a];7[a]	30	67	YES		YES	
2011	9[a]	30	57	YES	YES	YES	YES
2012	16[d];8[a];8[a]	30	81	YES	YES	YES	YES
2013	8[a]	30	75	YES	YES	YES	YES
2014	6[a]	30	67	YES	YES	YES	YES
2015	5[a];5[a]	30	60	YES	YES	YES	YES

[a] Pooled samples.
[b] Not available.
[c] Only available for 5 out of 19 mothers.
[d] Individual samples.
[e] Only available for 7 out of 9 mothers.

5 Analytical methods

5.1 Organochlorines and brominated flame retardants

The internal standards, CB-53 for chlorinated substances, Dechlorane®603 and ^{13}C-labelled BDE-155 and BDE-209 for brominated substances, were added to samples of 10 g human milk. The samples were extracted with a mixture of 2-propanol, n-hexane and diethyl ether according to the modified Jensen II extraction (Jensen et al. 2003, Sahlström et al. 2015). The organic phase was liquid/liquid partitioned with a solution of sodium chloride/phosphoric acid. The aqueous phase was re-extracted with n-hexane and the combined organic phases were evaporated to dryness in beakers. The lipid content was determined gravimetrically.

The lipids were dissolved in 3 ml isooctane and treated with concentrated sulfuric acid (Jensen et al., 1983). The organic phase was removed and the sulfuric acid was cleaned with an additional 1 ml isooctane to extract the remains. The combined organic phase after the sulfuric acid treatment was blown down to 0.6 ml of which 100 µl were used for the analysis of chlorinated substances and 500 µl were reduced to 100 µl and analysed for brominated substances.

Chlorinated substances, i.e. PCBs CB-28-CB-180, HCB, DDTpp and its breakdown products DDEpp and DDDpp as well as the insecticide γ-HCH (Lindane) and its α- and β-isomers were analysed on a gas chromatograph equipped with two EC-detectors. Two fused capillary columns were used in parallel: 60 m x 0.25 mm, film thickness 0.25 µm TG5MS respectively DB1701. Helium was used as carrier gas and Argon/Methane as make-up gas (Eriksson et al. 1997).

The brominated substances, BDE-47, -99,-100, -153, -154 and HBCDD, were analysed on a GC using a 30 m x 0.25 mm, I.D 0.25 µm TG5SilMS column connected to a mass spectrometer operating in electron capture negative ionization mode (NICI) (Sellström et al., 1998). BDE209 was analysed on a shorter TG5HT column, 15 m. DBE-DBCH(1,2-dibromo-4-(1,2 dibromoethyl) cyclohexane) was analysed using a TG5HT column as well but 30 m and with a thinner phase, 0.10 µm (Sahlström et al. 2015). Ammonia was used as reaction gas and the mass fragments m/z 79 and 81 were monitored. As quality check an internal control sample of pooled samples of mother´s milk were extracted in parallel as well as an internal control used at the National Food Agency, Sweden. The results were in accordance with previously obtained results.

Since data from earlier studies are included in the temporal trend analysis one sample analysed in a study by Bergman et al. 2010 was also analysed within this study to get an indication of the variability associated with the different analytical methods. For PCBs, DDTs, HCHs and HCB the re-analysis indicated only small differences between the two methods. For the PBDEs concentrations were slightly higher in the present study compared to Bergman et al. 2010, which could possibly be explained by differences in analytical method (Table 5.1).

Table 5.1. Reanalysis of one sample analysed in the study by Bergman et al. 2010 in ng/g fat.

Substance	Bergman et al. 2010	Present study
HCB	8	9
β-HCH	8	6
DDE	69	58
DDT	5	4
CB-118	7	4
CB-153	30	25
CB-138	24	13
CB-180	16	11
BDE-28	0.10	0.096
BDE-47	0.72	1.1
BDE-99	0.11	0.19
BDE-100	0.18	0.3
BDE-153	0.29	0.42
BDE-154	0.023	-99.99

5.2 Dioxins, dibenzofurans and dioxin-like PCBs

PCDD/Fs and dl-PCBs (PCB 77, 81, 105, 114, 118, 123, 126, 156, 157, 167, 169, and 189) were analysed at the National Food Agency using a previously described method (Aune et al. 2012). Briefly, the milk samples were extracted with a combination of organic solvents and the lipid weight was determined gravimetrically. Clean-up and fractionation steps were performed on a PowerPrep™-system from Fluid Management Systems (MA, USA). Finally, the samples were quantified using gas chromatography coupled to high resolution mass spectrometry (GC-HRMS) with isotope dilution technique. The HRMS was operated in EI mode, using single ion monitoring (SIM) at the resolution of 10 000.

All samples were fortified with ^{13}C-labelled internal standards for all congeners prior to extraction to correct for analytical losses and to ensure quality control. A number of control samples were analysed together with the samples to verify the accuracy and precision of the measurements. The laboratory is accredited for analysis of PCBs and PCDD/Fs in human milk.

5.3 Perfluorinated substances

Analysis of per- and polyfluoroalkyl substances (PFASs; Table 5.1), in human milk samples were carried out using UPLC coupled to a Xevo TQ-S triple quadrupole mass spectrometer (Waters) operated in negative ion electrospray ionization, (ESI−) selected reaction monitoring (SRM) mode. Extracts were chromatographed on a BEH C18 analytical column (2.1×50mm, 1.7 μm particle size, Waters) operated at a flow rate of 0.4 ml/min, using a mobile phase composition of 90 % water/10 % acetonitrile containing 2 mM ammonium acetate (solvent A) and 100 % acetonitrile containing 2 mm ammonium acetate (solvent B). A total of two precursor/product ion transitions were monitored in the analyte; one for quantification and the other for qualification.

Quantitative determination of target compounds was carried out by isotope dilution or an internal standard quantification approach using a linear calibration curve with 1/X weighting. Branched isomers were determined semi-quantitatively using the calibration curve for the linear isomer. For all targets with the exception of PFOA, the primary ion was used for quantification. For PFOA, the m/z 413/169 ion was used for quantification because of an interference in the m/z 413/369.

Milk samples were extracted using a modified version of the Olsen et al 2007 involving a back extraction technique (Sundström et al. 2011). Briefly, the initial extraction of approximately 2 ml of sample was accomplished at acidic pH by adding 600 µl of 1N formic acid followed by 50 µl of stable isotope-labelled internal standards (concentration of internal standards provided around 20 pg/µl). The tube was vortexed, then 600µl of saturated ammonium sulfate was added, and the tube was vortexed again. Acetonitrile (7ml) was added and the tubes were placed on a mechanical shaker for 30 minutes followed by centrifugation. The top organic layer containing the analytes of interest was transferred into a polypropylene tube and evaporated at 40˚C. The aqueous residual from the primary extraction was diluted with 300 µl of pure water and vortexed before adding 500 µl of 1N potassium hydroxide. The tube was vortexed, after which 7 ml of methyl tert-butyl ether was added. The tube was placed on a mechanical shaker for 20 minutes followed by centrifugation and transfer of the top organic layer containing the analytes of interest, into a clean polypropylene tube. The extracts were evaporated at 40˚C. After evaporation, 200 µl of buffer (0.1 M ammonium acetate:acetonitrile:purified water= 1:2:1) was added to the residual and the sample was vortexed and centrifuged. Lipids partitioned to the top layer, while the lower layer contained buffer and the analytes of interest. The lower layer was transferred to microvial for analysis by UPLC-MS/MS.

Standards and suppliers are provided in Table 5.2.

Table 5.2. Analytes of interest included the native, surrogate standards and the supplier.

Target Class	Target Compounds	Acronym[1]	Native		Surrogate	
			Standard	Supplier	Standard	Supplier
PFCAs	Perfluorobutanoic acid	L-PFBA	L-PFBA		$^{13}C_4$-PFBA	
PFCAs	Perfluoropentanoic acid	L-PFPeA	L-PFPeA		$^{13}C_5$-PFPeA	
PFCAs	Perfluorohexanoic acid	L-PFHxA	L-PFHxA		$^{13}C_2$-PFHxA	
PFCAs	Perfluoroheptanoic acid	L-PFHpA	L-PFHpA		$^{13}C_4$-PFHpA	
PFCAs	Linear Perfluorooctanoic acid	L-PFOA	L-PFOA		$^{13}C_4$-PFOA	
PFCAs	Branched Perfluorooctanoic acid	B-PFOA	L-PFOA	Well Labs	$^{13}C_4$-PFOA	Well Labs
PFCAs	Perfluorononanoic acid	L-PFNA	L-PFNA		$^{13}C_5$-PFNA	
PFCAs	Perfluorodecanoic acid	L-PFDA	L-PFDA		$^{13}C_2$-PFDA	
PFCAs	Perfluoroundecanoic acid	L-PFUnDA	L-PFUnDA		$^{13}C_2$-PFUnDA	
PFCAs	Perfluorododecanoic acid	L-PFDoDA	L-PFDoDA		$^{13}C_2$-PFDoDA	
PFCAs	Perfluorotridecanoic acid	L-PFTrDA	L-PFTrDA		$^{13}C_2$-PFDoDA	
PFCAs	Perfluorotetradecanoic acid	L-PFTeDA	L-PFTeDA		$^{13}C_2$-PFDoDA	
PFCAs	Perfluoropentadecanoic acid	L-PFPeDA	L-PFTeDA		$^{13}C_2$-PFDoDA	
PFSAs	Perfluorobutane sulfonic acid	PFBS	L-PFBS		$^{13}C_2$-PFHxA	
PFSAs	Linear Perfluorohexane sulfonic acid	L-PFHxS	L-PFHxS		$^{18}O_2$-PFHxS	
PFSAs	Branched Perfluorohexane sulfonic acid	B-PFHxS	L-PFHxS		$^{18}O_2$-PFHxS	
PFSAs	Linear Perfluorooctane sulfonic acid	L-PFOS	L-PFOS		$^{13}C_4$-PFOS	
PFSAs	Branched Perfluorooctane sulfonic acid	B-PFOS	L-PFOS		$^{13}C_4$-PFOS	
PFSAs	Linear Perfluorodecane sulfonic acid	L-PFDS	L-PFDS		$^{13}C_2$-PFUnDA	
PFSAs	Branched Perfluorodecane sulfonic acid	B-PFDS	L-PFDS		$^{13}C_2$-PFUnDA	
FASAs	Linear Perfluorooctane sulfonamide	L-FOSA	L-FOSA	Well Labs	$^{13}C_8$-FOSA	Well Labs
FASAs	Branched Perfluorooctane sulfonamide	B-FOSA	L-FOSA		$^{13}C_8$-FOSA	
FASAs	Linear Perfluorooctane sulfonamidoacetic acid	L-FOSAA	L-FOSAA		d3-MeFOSAA	
FASAs	Branched Perfluorooctane sulfonamidoacetic acid	B-FOSAA	L-FOSAA		d3-MeFOSAA	
FASAs	Linear N-Methyl Perfluorooctane sulfonamidoacetic acid	L-MeFOSAA	L-MeFOSAA		d3-MeFOSAA	
FASAs	Branched N-Methyl Perfluorooctane sulfonamidoacetic acid	B-MeFOSAA	L-MeFOSAA		d3-MeFOSAA	
FASAs	Linear N-Ethyl Perfluorooctane sulfonamidoacetic acid	L-EtFOSAA	L-EtFOSAA		d5-EtFOSAA	
FASAs	Branched N-Ethyl Perfluorooctane sulfonamidoacetic acid	B-EtFOSAA	L-EtFOSAA		d5-EtFOSAA	
	Recovery Standards					
	$^{13}C_8$ labeled Perfluorooctanoic acid	M8-PFOA		Well Labs		
	$^{13}C_8$ labeled Perfluorooctane sulfonic acid	M8-PFOS		Well Labs		

6 Data handling

6.1 Data included in the analysis

Data from earlier studies in human milk from Stockholm and Gothenburg have been included in the trendanalysis if available. Data (years) from this study are presented in Table 4.1 and data belonging to other studies are found in the result section in respective chapter.

6.2 Temporal trends

One of the main objectives of the monitoring programme is to detect temporal trends. Trend detection is in general carried out in three steps.

6.2.1 Log-linear regression analyses

Log-linear regression analyses are performed for the entire investigated time period and also for the most recent ten years for longer time series.

The slope of the line describes the yearly percentage change. A slope of 5 % implies that the concentration is halved in 14 years, whereas a slope of 10 % corresponds to a similar reduction in 7 years, and 2 % in 35 years (Table 6.1).

Table 6.1. The approximate number of years required to double or half the initial concentration, assuming a continuous annual change of 1, 2, 3, 4, 5, 7, 10, 15 or 20 % a year.

	1%	2%	3%	4%	5%	7%	10%	12%	15%	20%
Increase	70	35	24	18	14	10	7	6	5	4
Decrease	69	35	23	17	14	10	7	6	4	3

6.2.2 Non-parametric trend test

The regression analysis presumes, among other things, that the regression line gives a good description of the trend. The leverage effect of points at the end of the line is a well-known fact. An exaggerated slope, caused ‘by chance’ by a single or a few points at the end of the line increases the risk of a false significant result when no real trend exist. A non-parametric alternative to the regression analysis is the Mann-Kendall trend test (Gilbert 1987, Helsel D.R. and Hirsch R.M. 1992, International Council for the Exploration of the Sea 1995).

6.2.3 Non-linear trend components

An alternative to the regression line used to describe development over time is a type of smoothed line. The smoother applied here is a simple 3-point running mean smoother fitted to the annual geometric mean values. In cases where the regression line is a poor fit, the smoothed line may be more appropriate. The significance of this line is tested using an ANOVA, where the variance explained by the smoother and the regression line is compared with the total variance. This procedure is described by Nicholson et al. (Nicholson et al. 1998).

In addition, non-linear trends could also be investigated using Change-Point detection. A method suggested by Sturludottir et al. (2015) which iteratively searches for a combination of two log-linear regression lines with different slopes that explains significantly more of the total variance than what is explained by a single regression line for the whole study period. This method was here used to investigate perfluorinated substances which has been analysed by the same laboratory during the whole monitoring period.

6.2.4 Plot Legends

Each figure displays the mean concentration of each year (circles) together with the individual analyses (small dots) and the 95% confidence intervals of the geometric means.

The trend for the whole time period is presented by a regression line (plotted if $p < 0.10$, two-sided regression analysis); $p < 0.05$ is presented by a red line and $0.05 < p < 0.10$ is presented by a dashed blue line. The trend for the last ten years is plotted if $p < 0.2$ and $p < 0.05$ is presented by a red line and $0.05 < p < 0.2$ is presented by a dashed light blue line. Ten years is often a too short period to statistically detect a trend unless it is of considerable magnitude. Nevertheless, the ten year regression line will indicate a possible change in the direction of a trend.

A smoother is applied to test for non-linear trend components (see section 6.2.3). The smoothed line is plotted if $p < 0.10$ and $p < 0.05$ is presented by a red line and $0.05 < p < 0.10$ is presented by a dashed blue line. A broken line segment indicates a gap in the time series with a missing year.

The log-linear regression lines fitted through the geometric mean concentrations follow smooth exponential functions.

A cross inside a circle indicates a suspected outlier from a log-linear trend (see section 6.4).

n(tot)= first line reports the total number of analyses included together with the number of years (**n(yrs)=**);

slope= reports the slope, expressed as the yearly percentage change together with its 95 % confidence interval;

CV(lr)= reports the coefficient of variation around the regression line, as a measure of between-year variation, together with the lowest detectable change (given in percent per year) in the current time series with a power of 80 %, one-sided test, α=0.05. The last figure on this line is the estimated number of years required to detect an annual change of 10 % with a power of 80 %, one-sided test, α=0.05.

power= reports the power to detect a log-linear trend in the time series (Nicholson and Fryer 1992). The first number represents the power to detect an annual change of 5 % with the number of years in the current time series. The second number is the power estimated as if the slope where 5 % a year and the number of years were ten. The third number is the lowest detectable change (given in percent per year) for a ten year period with the current between-year variation at a power of 80 %.

y(14/15)= reports the concentration estimated from the regression line for the last year together with a 95 % confidence interval;

r^2= reports the coefficient of determination (r^2) together with a p-value for a two-sided test;

tao= reports Kendall's '**τ**', and the corresponding p-value;

CV(sm)= reports the coefficient of variation around the smoothed line and the p-value. A significant result will indicate a non-linear trend component. After the p-value, the minimum trend (percentage per year) likely to be detected at a power of 80 % during a period of 10 years, should a log-linear trend occur, is shown. This estimate is compensated for the loss of degrees of freedom, considering the smoother. Requires five years or more of data to be calculated;

y(14/15)= reports the concentration estimated from the smoothed line for the last year together with a 95 % confidence interval. Requires five years or more of data to be calculated.

Below these nine lines are additional lines with information concerning the regression for the last ten years.

6.3 Principal Component Analysis and F-test

Principal Component Analysis (PCA) was performed on the proportion of the individual substances concentrations within a group to the ∑PFASs, ∑PBDEs/HBCDD, ∑PCBs, ∑PCDDs/PCDFs/dl-PCBs to study difference in patterns between Stockholm and Gothenburg (2007-2015). Only substances with more than 50 % of the results above LOQ were included in this analysis.

An F-test was used to test if the variances differed significantly between the samples with regard to individual measurements of PFASs from Stockholm and Gothenburg in 2012. Only PFASs with more than 50 % of the results above LOQ were included in this analysis.

6.4 Outliers and values below the detection limit

Observations further from the regression line than what is expected from the residual variance around the line are subject to special concern. These deviations may be caused by an atypical occurrence of something in the physical environment, a changed pollution load, or errors in the sampling or analytical procedure. The procedure to detect suspected outliers in this context is described by Hoaglin and Welsch (Hoaglin and Welsch 1978). The suspected outliers are merely indicated in the figures and are included in the statistical calculations.

Values reported that are below the quantification limit are substituted using the reported LOQ divided by the square root of 2 for ClCs, BFRs and PFASs. This is not the case for ∑PCDDs, ∑PCDFs and ∑dl-PCBs in WHO-TEQ_{2005} concentrations, for which the analytical labratory have calculated using LOQ divided by 2.

7 Pollutant regulation: conventions and legislation

7.1 The Stockholm Convention on Persistent Organic Pollutants

The Stockholm Convention on Persistent Organic Pollutants (POPs) is an international agreement requiring measures for reducing or preventing release of dangerous substances into the environment. The Stockholm Convention was adopted in 2001 and entered into force in 2004. The convention deals with organic compounds that are persistent and remain in the environment for a long time, have a potential for long-range transport, bioaccumulate in fatty tissues of organisms, and have adverse effects on human health or the environment. Initially, 12 chemicals were included in the treaty in 2001 (aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, mirex, toxaphene, PCB, hexachlorobenzene, polychlorinated dibenzo-p-dioxins, polychlorinated dibenzofurans). In May 2009, an amendment was adopted into the convention, and nine additional chemicals were listed as POPs (hexa-/heptabromdiphenylether, tetra-/pentabromodiphenylether, chlordecone, hexabromobiphenyl, lindane, α- and β –hexachlorocyklohexane, pentachlorobenzen and PFOS).
In May 2011 an amendment was adopted into the convention and technical endosulfan and its related isomers were added to the list with specific exemptions. Since November 2014, hexabromocyclododecane (HBCDD) is also included in the Stockholm Convention. Six more substances have been nominated to be included on the list, and are currently under review by the Persistent Organic Pollutants Review Committee; decabromodiphenyl ether (commercial mixture, "c-decaBDE"), dicofol, short-chained chlorinated paraffins (SCCPs), chlorinated naphthalenes, hexachlorobutadiene and pentachlorophenol (SC 2008).

7.2 The Convention on Long-Range Trans boundary Air Pollution

The Convention on Long Range Trans boundary Air Pollution (CLRTAP) was initiated in 1972 at a United Nations Conference on the Human Environment in Stockholm. After the scientific findings that acidification in Swedish lakes was caused by sulphur emission from continental Europe, the necessity for international measures to reduce emissions to air that had environmental effects far from its source, was addressed. In 1979, the convention was signed in Geneva, and entered into force in 1983. Initially, the convention focused on sulphuric compounds causing acidification, but later eight protocols were added for other groups of substances e.g., nitrogen oxides, volatile organic compunds (VOCs) and persistent organic pollutants (POPs) (http://www.unece.org/env/lrtap/lrtap_h1.htm).

7.3 EU chemical legislation

7.3.1 REACH

REACH is the EU chemicals policy that entered into force on the 1st of June 2007 (The European Parliament and The European Council, 2006). REACH stands for Registration, Evaluation, Authorization and Restriction of Chemical Substances. The policy places more responsibility on industry, and importers and users have to gather information about their chemicals, which they then report to the European Chemicals Agency (ECHA) situated in Helsinki. ECHA manages REACH by gathering information and keeping databases of chemicals used in the EU (The European Commision 2007).

7.3.2 RoHS directive

The Directive on the Restriction of Hazardous Substances (RoHS) was adopted in February 2003. The RoHs directive reduces the use of six chemical substances in electrical or electronic products that were released on the market after July 2006. These substances are mercury, cadmium, lead, chromium VI, polybrominated biphenyls and polybrominated diphenyl ethers. The maximum allowed amount of these substances (based on weight) is 0.01 % for cadmium, and 0.1 % for the other substances (KEMI 2011).

7.4 Swedish chemical legislation

One of the 16 Swedish environmental quality objectives is "A non-toxic environment", which means that concentrations of non-naturally occurring substances should be close to zero, and naturally occurring substances should be close to background concentrations. Their impact on human health and ecosystems should be negligible (KEMI 1999). The agency responsible for coordinating this work is the Swedish Chemicals Agency (KEMI). The Swedish chemical legislation follows EU legislation. Much of the national legislations that existed before June 2007 were replaced by REACH (KEMI).

8 Fat Content

8.1 Results

The fat content was specified both for the analysis of ClCs /BFRs and dioxins. Only the fat content measured during the dioxin analysis was evaluated since over time CLCs/BFRs have been analysed by more than three different laboratories and dioxins only by two. Data on fat content from Fång et al. 2013 was included in the evaluation of temporal trend for fat content.

Table 8.1 Trend for the entire period (and the last 10 year period for Stockholm) (in %) for **fat content** assessed from the annual means (%) in human milk from Stockholm and Gothenburg. P shows the p-value, YRQ: years required to detect an annual change of 10 % with a power of 80 % and LDT: lowest detectable trend (given in percent per year) for a ten year period with the current between-year variation at a power of 80 %. Last year's fat contents are estimated from the smoothed trend. Numbers in brackets are 95 % confidence intervals (C.I.). The total number of samples and the number of years for the various time-series are shown in columns two and three.

Sampling site	N samples	N years	Period (Years)	Trend % (95 % C.I.)	P	YRQ	LDT %	Last year % (95 % C.I.)
Stockholm	35	25	72-14	0.62(.26,.97)	**0.001**	7	4.6	3.17(3.04, 3.32)
Stockholm	16	8	07-14	-3.7(-6.8,-.50)	**0.030**	6	3.6	
Gothenburg	14	7	07-15	2.7(-.91,6.4)	0.119	7	4.3	3.63(3.29, 4.00)

8.1.1 Temporal trends

Fat content in human milk from Stockholm show a significant upward trend during the time period 1972–2014 (Table 8.1 and Figure 8.1) an annual mean increase of 0.62%. In contrast a significant downward trend is seen for the 10 most recent years of -3.7 % per year. However, the temporal trend is based on analysis of fat content from two laboratories (1972-2011 and 2012-2014) and the downward trend could possibly be caused by differences in the analytical method between the two laboratories (Figure 8.1) since the fat content seemed to have dropped the same year as the change in analytical laboratory occurred. An upward trend is indicated for the fat content in human milk from Gothenburg (2007-2015) with an increase of on average 2.7 % per year.

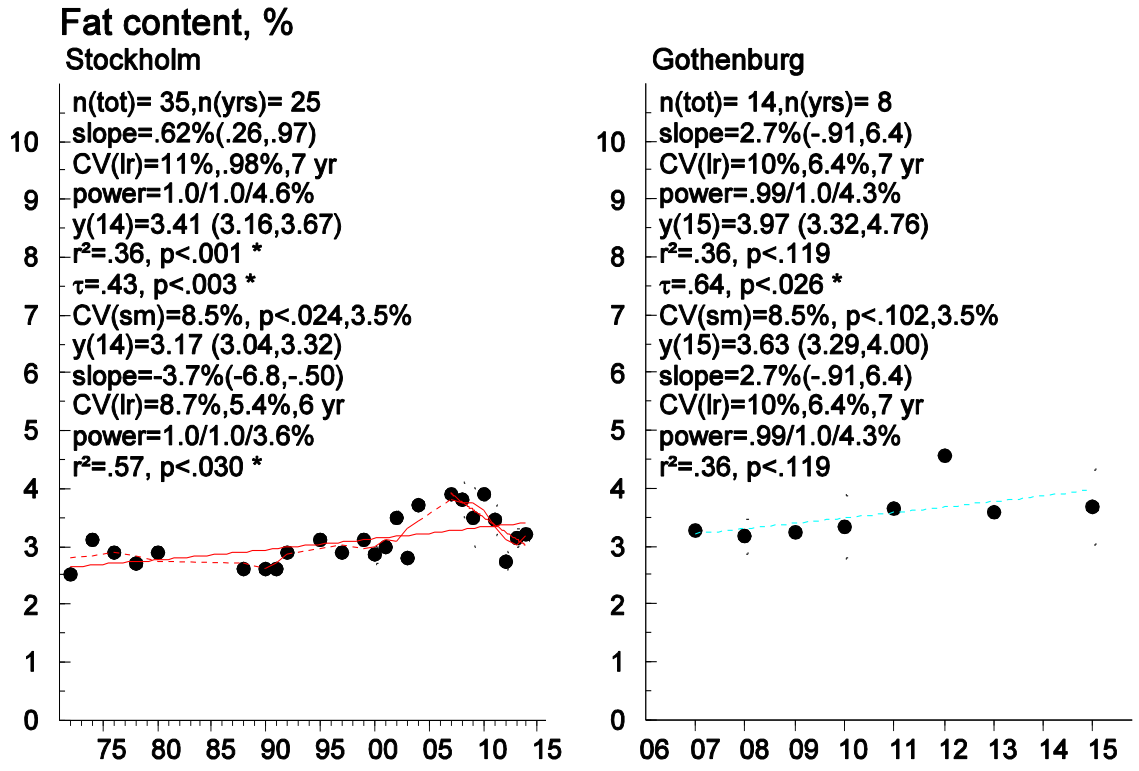

Figure 8.1. Temporal trend of lipid content in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015).

8.1.2 Spatial differences

The fat content is not only affected by time post-partum (fat content increases with increasing time post-partum), but also by the portion of feeding (fat content increases during the course of a single feeding), number of children, and infections (La Kind 2002). The fat content in 2014/2015 estimated from the smoothed line is in Stockholm (3.2 %) and in Gothenburg (3.6 %). A study by Jensen et al. (1996) reports an average fat content of 3-5 % and similar numbers are also reported by Mitoulas et al. (2002) which is coherent with the fat content measured in the present study. The mean lipid content (2008-2014) in the Uppsala cohort was lower than in the present study (mean 2.8 %, range 1.46-5.91 %) (M Aune 2017, pers comm., 7 June).

8.2 Conclusion

The fat content in human milk from Stockholm is increasing significantly during the whole monitoring period (0.62 % per year). The fat content in human milk from Stockholm and Gothenburg is in the same range as fat content in human milk reported in other studies from different parts of the world.

9 Polychlorinated biphenyls

9.1 Introduction

Polychlorinated biphenyls (PCBs) consist of two linked phenyl rings substituted with one or more chlorine atoms. Out of a possible 209 congeners, depending on the number and position of the chlorine atoms, 20 have non-ortho chlorine substitutions and can thus attain a planar structure. Similar to the highly toxic polychlorinated dibenzo-p-dioxins and dibenzofurans (Mckinney et al. 1985). Production of technical polychlorinated biphenyls (PCBs) started in 1929. Due to its chemical and physical properties (e.g. heat resistance) this group was mainly used in transformers, capacitors, hydraulic liquids and lubricants (UNEP 2016). The open use of PCBs have been nationally (SFS 1971:385) and internationally banned since the early 1970s, followed by a ban of all new uses in 1978, and finally, the total ban of PCBs in Sweden in 1995 (SFS 1995: 1095).

9.2 Results

The PCB congeners analysed within this study from Stockholm (2010-2014) and Gothenburg (2011-2015) were CB-28, CB52, CB-101, CB-118, CB-138, CB-153 and CB-180. For CB-52 and CB-101 all measurements were below LOQ except for in one sample from Stockholm in 2010, where the concentrations were 27 and 31 ng/g fat, respectively. Additional data for CB-153 and CB-118 from Lundén and Norén 1998, Athanasiadou and Bergman 2008 and Bergman et al. 2010 and for CB-138 and CB-180 from Bergman et al. 2010, were also included in the temporal trend analysis.

Table 9.1 Trend for the entire period (and the last 10 year period for Stockholm) for **CB-180, CB-153, CB-138, CB-118 and CB-28** assessed from the annual means (ng/g fat) in human milk from Stockholm and Gothenburg. P shows the p-value, YRQ: years required to detect an annual change of 10 % with a power of 80 % and LDT: lowest detectable trend (given in percent per year) for a ten year period with the current between-year variation at a power of 80 %. Last year's concentration is estimated from the smoothed trend. Numbers in brackets are 95 % confidence intervals (C.I.). The total number of samples and the number of years for the various time-series are shown in columns two and three.

Substance	Sampling site	N samples	N years	Period (Years)	Trend % (95 % C.I.)	P	YRQ	LDT %	Last year ng/g l.w. (95 % C.I.)
CB-180	Stockholm	17	8	07-14	-13(-16,-8.9)	**0.001**	7	4.5	8.07(7.07,9.22)
	Gothenburg	35	7	08-15	-9.1(-12,-5.6)	**0.001**	6	3.6	9.96(8.60,11.5)
CB-153	Stockholm	29	18	72-14	-5.6(-6.5,-4.5)	**0.001**	12	13	16.7(15.0,18.7)
	Stockholm		8	07-14	-12(-20,-4.2)	**0.011**	10	10	
	Gothenburg	35	7	08-15	-5.9(-9.7,-1.9)	**0.013**	7	3.9	21.8(18.8,25.3)
CB-138	Stockholm	17	8	07-14	-14(-19,-9.0)	**0.001**	8	6.4	9.65(7.73,12.0)
	Gothenburg	35	7	08-12	-13(-18,-7.5)	**0.002**	8	6.2	11.4(9.28,14.1)
CB-118	Stockholm	28	17	72-14	-6.0(-6.6,-5.5)	**0.001**	8	6.5	3.27(2.88,3.73)
	Stockholm		8	07-14	-9.8(-16,-3.0)	**0.013**	9	8.2	
	Gothenburg	35	7	08-15	-12(-18,-6.6)	**0.003**	8	6.2	3.33(2.67,4.16)
CB-28	Stockholm	10	5	10-14	-1.4(-45,85)	0.947	18	31	1.04(0.313,3.49)
	Gothenburg	7	4	11-15	-9.6(-21,3.0)	0.081	7	3.8	0.778(0.545,1.11)

9.2.1 Temporal variation

The concentrations of the congeners CB-153 and CB-118 in human milk from Stockholm decreased significantly during the time period 1972–2014 (Figure 9.1, 9.2 and Table 9.1),

with an annual mean decrease of -5.6% and -6.0% respectively. CB-180, CB-153, CB-138 and CB-118 in human milk from both Stockholm and Gothenburg showed significant downward trends during the most recent 10 year period of -5.9 to -14 % per year, but no trend could be detected for CB-28 (Figure 9.1, 9.2 and Table 9.1). However, CB-28 was only analysed for 4/5 years (Gothenburg and Stockholm) and in 6 out of 17 of the samples the measurements of CB-28 were below LOQ (Table 9.1).

The temporal trend for CB-153 in human milk reported in this study was of similar magnitude as the temporal trends reported by Konishi et al. 2001 (Japan, 1972-1998) and Lignell et al. 2014 (Uppsala, 1996-2012), which showed significant decreasing concentrations of -7.5 % and -7 %, respectively. The trend for CB-153 in this study also coincides with the trends seen in Swedish marine (Bignert et al. 2017) and freshwater (Nyberg et al. 2016) biota for the whole monitoring period. However, during the most recent 10 year period the concentration in human milk from Stockholm seems to decrease at a faster rate than in biota. This might be a result of the dietary advice set by the Swedish Food Agency to protect fertile and pregnant women against food (especially fat fish from the Baltic) that contains high levels of POPs.

The number of years required to detect an annual change of 10 % for CB-180, CB-153, CB-138 and CB-118 varied between 6-12 years.

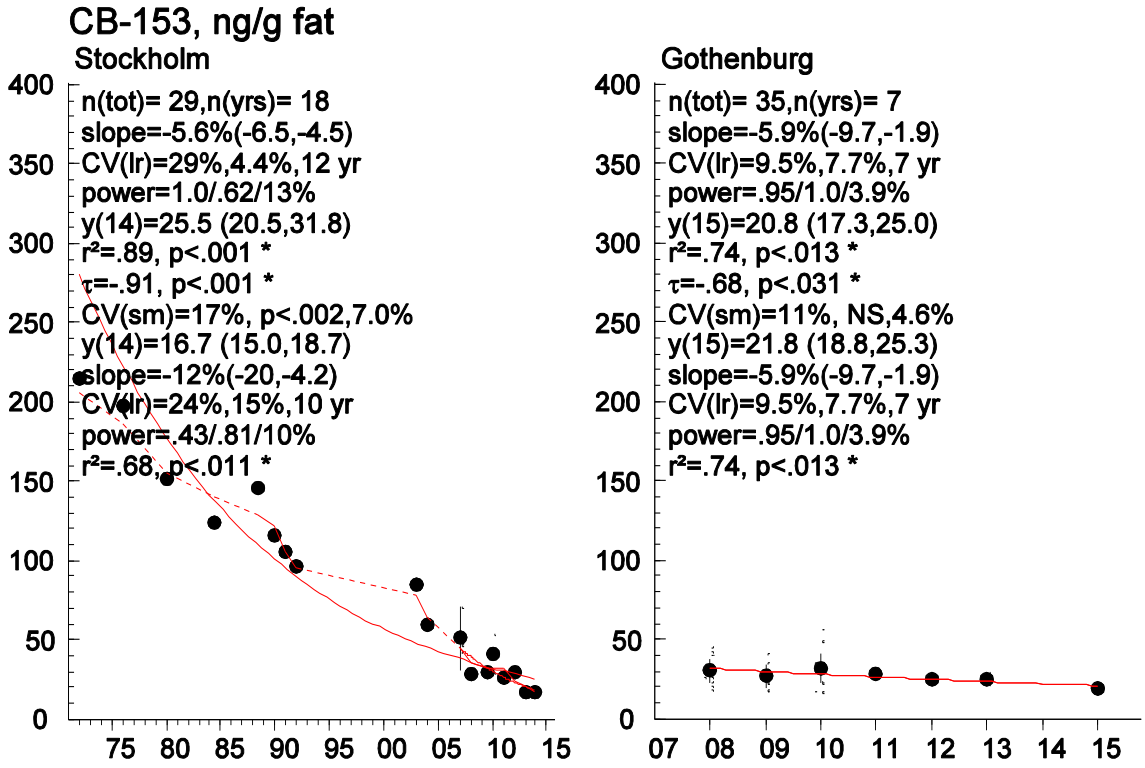

Figure 9.1 Temporal trend of CB-153 (ng/g fat) in human milk from Stockholm (1972-2014) and Gothenburg (2008-2015).

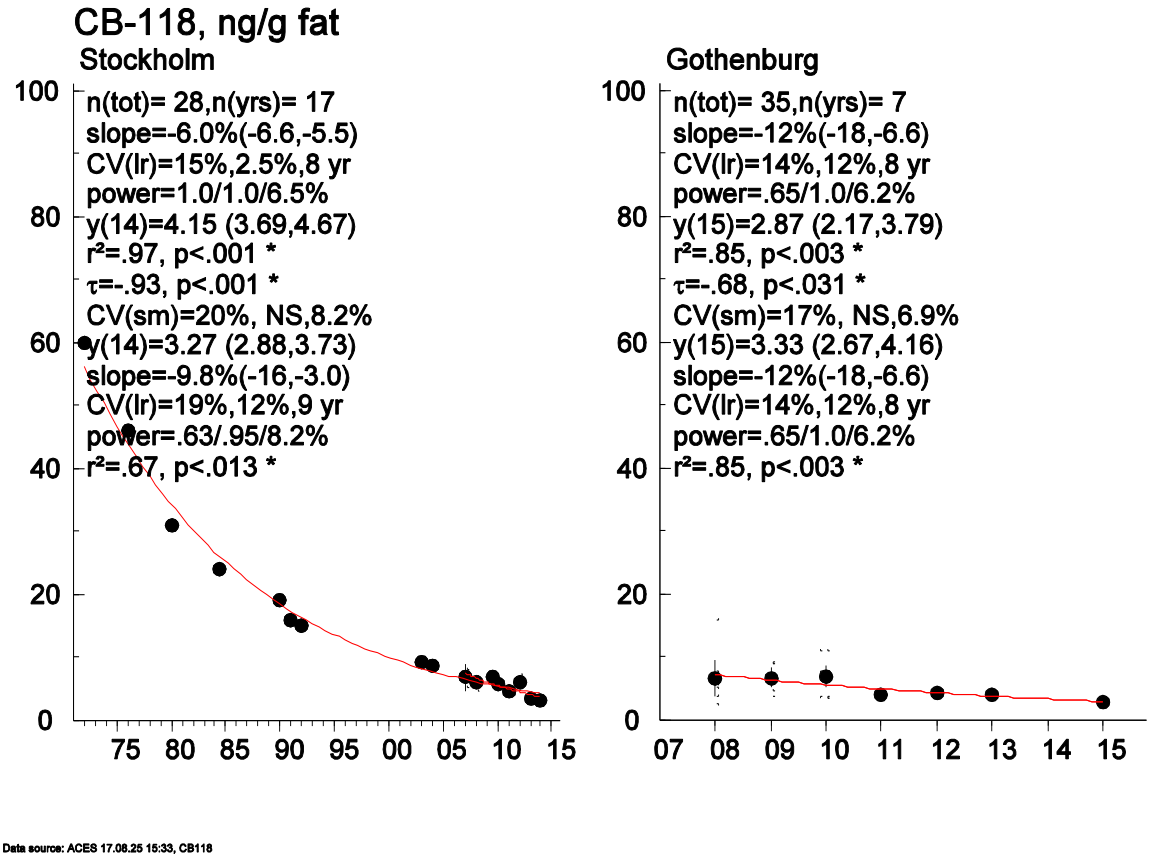

Figure 9.2 Temporal trend of CB-118 (ng/g fat) in human milk from Stockholm (1972-2014) and Gothenburg (2008-2015).

9.2.2 Concentrations and spatial differences

The concentration of CB-153 in 2014/2015 estimated from the smoothed line was in Stockholm 17 ng/g fat and in Gothenburg 22 ng/g fat. These concentrations were somewhat lower than concentrations reported for other European countries (26-900 ng/g fat) in a review by Fång et al. 2015. However, the studies from the review were published between1995-2011 and the concentrations are expected to be higher back in time closer to the ban of PCBs. Lignell et al. 2014 reported a mean concentrations of 22 ng/g fat for CB-153 in human milk from Uppsala (2012), which was very close to the concentrations reported here. The concentrations of CB-180, CB-138, CB-118 and CB-28 reported in the Uppsala study were also comparable to the concentrations reported in this study.

The PCA (Figure 9.3) show a tendency of higher relative average concentrations of CB-180 in Gothenburg and higher relative average concentrations of CB-118 and CB-138 in Stockholm, but there was no significant difference in PCB congener pattern between Stockholm and Gothenburg (2011-2015).

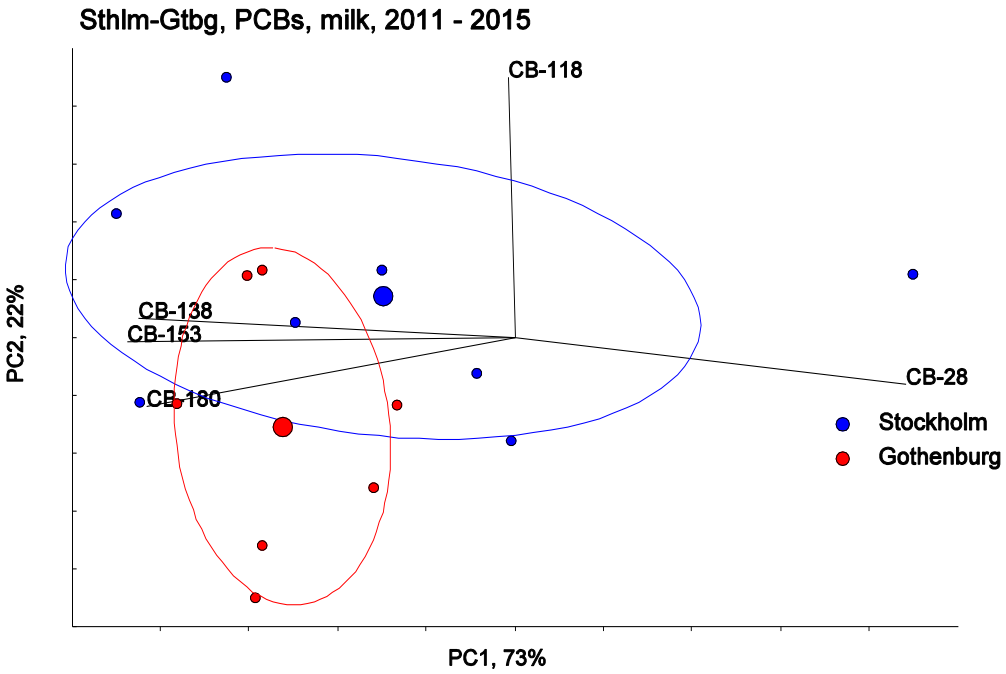

Figure 9.3 PCA (principal component analysis), biplot and Hotellings 95 % confidence ellipses for center of gravity for each group. The figure shows the CB-180, CB-153, CB-138, CB-118 and CB-28 in human milk from Stockholm and Gothenburg (2011-2015).

9.3 Conclusion

The concentrations of the congeners CB-180, CB-153, CB-138 and CB-118 in human milk from Stockholm and Gothenburg decreased significantly during the whole monitoring period and during the most recent ten year period. The concentrations reported here are comparable to concentrations reported from other countries in Europe. There was no significant difference in PCB congener pattern between Stockholm and Gothenburg.

10 Dichlorodiphenylethanes, Hexachlorocyclohexanes, Hexachlorobenzene

10.1 Introduction

Dichlorodiphenyltrichloroethane (DDT) is a potent insecticide that has mainly been used for mosquito control (UNEP 2016). DDT is transformed to dichlorodiphenyldichloroethylene (DDE) and dichlorodiphenyldichloroethane (DDD). The use of DDT has been banned since the 1970s in most countries. Currently it is only allowed to combat malaria (UNEP 2016), primarily in Africa and the Pacific Islands (Bogdal et al. 2013).

Hexachlorobenzene (HCB) has primarily been used as a fungicide and has been banned in the Baltic countries since mid-1970s (Gaul 1992). HCB is also formed as a by-product in a number of industrial processes (e.g. electrolyte production, chlor-alkali processes, and waste incineration of materials containing chlorine), thus can still enter the environment (WHO 1997, Garı´ et al. 2014).

Hexachlorocyclohexane (HCH) has been produced since the late 1940s. Three of its isomers are of environmental interest, specifically α-, β- and γ-HCH. γ-HCH, known as lindane, is the most potent HCH isomer of this group; however, the technical mixtures of all three isomers have been widely used as commercial pesticides. The use of HCHs has been regulated or banned in a number of countries since the 1970-1990s (Willett et al. 1997). However, China and Romania did not cease lindane production until recently, while in India, lindane is still produced (Vijgen et al. 2011).

10.2 Results

DDT, DDE, DDD, α-, β- and γ-HCH and HCB were analysed in human milk samples from Stockholm (2010-2014) and Gothenburg (2011-2015). For DDD, α- and γ-HCH all measurements were below LOQ. Additional data for DDE, DDT and HCB from Lundén and Norén 1998, Athanasiadou and Bergman 2008 and Bergman et al. 2010 and for β-HCH from Bergman et al. 2010, were also included in the temporal trend analysis.

Table 10.1 Trend for the entire period (and the last 10 year period) (in %) for **DDE, DDT, HCB and β-HCH** assessed from the annual means (ng/g fat) in human milk from Stockholm and Gothenburg. P shows the p-value, YRQ: years required to detect an annual change of 10 % with a power of 80 % and LDT: lowest detectable trend (given in percent per year) for a ten year period with the current between-year variation at a power of 80 %. Last year's concentration is estimated from the smoothed trend. Numbers in brackets are 95 % confidence intervals (C.I.). The total number of samples and the number of years for the various time-series are shown in columns two and three.

Substance	Sampling site	N samples	N years	Period (Years)	Trend % (95 % C.I.)	P	YRQ	LDT %	Last year ng/g l.w. (95 % C.I.)
DDE	Stockholm	27	18	72-14	-7.9(-8.9,-7.0)	**0.001**	12	13	49.8(42.0,59.1)
	Stockholm		8	07-14	-6.8(-19,-6.6)	0.246	13	17	
	Gothenburg	35	7	08-15	-7.1(-13,-.65)	**0.037**	8	6.6	39.4(30.8,50.4)
DDT	Stockholm	27	18	72-14	-11(-13,-9.8)	**0.001**	15	22	2.94(2.30,3.78)
	Stockholm		8	07-14	-8.1(-17,2.1)	0.097	11	13	
	Gothenburg	35	7	08-15	-12(-16,-8.5)	**0.001**	7	2	2.28(1.89,2.75)
HCB	Stockholm	27	18	72-14	-7.2(-9.0,-5.4)	**0.001**	16	26	7.69(5.79,10.2)
	Stockholm		8	07-14	-.77(-6.9,5.8)	0.776	9	7.3	
	Gothenburg	35	7	08-15	2.1(-.77,5.1)	0.119	6	2.7	8.45(7.81,9.13)
β -HCH	Stockholm	17	8	07-14	-13(-38,20)	0.326	22	52	2.42(0.849,6.92)
	Gothenburg	35	7	08-15	-19(-26,-12)	**0.001**	10	8.6	2.07(1.58,2.70)

10.2.1 Temporal variation

The concentrations of DDT, its metabolite DDE and HCB in human milk from Stockholm decreased significantly during the time period 1972–2014 (Figure 10.1, 10.2, 10.3 and Table 10.1), with an annual mean decrease of -7.2 to -11 %. No trend was observed for β-HCH in the milk from Stockholm, however, the monitoring period was short (2007-2014) and two of the measurements in 2009 and 2012 were high compared to the others (25 and 56 ng/g fat) which probably affected the ability to detect a trend (Figure 10.4 and Table 10.1). DDE, DDT and β-HCH also showed significant downward trends in human milk from Gothenburg of -7.1, -14 and -19 % per year, respectively (Figure 10.1, 10.2, 10.3, 10.4 and Table 10.1). In contrast, concentrations in human milk from Stockholm seemed to have levelled out during the most recent ten year period.

The temporal trend for DDE in human milk reported in this study was of similar magnitude as the temporal trends reported by Konishi et al. 2001 (Japan, 1972-1998) and Lignell et al. 2014 (Uppsala, 1996-2012), which showed significant downward trends of -9.1 % and -7.4 %, respectively. The temporal trend for HCB also coincides with the downward trend reported by Lignell et al. 2014 of -5.9 %. The trends for DDE, DDT and HCB in this study were also in good agreement with the trends seen in Swedish marine (Bignert et al. 2017) and freshwater (Nyberg et al. 2016) biota for the whole monitoring period.

The number of years required to detect an annual change of 10 % for DDE, DDT, HCB and β-HCH varied between 7-22 years.

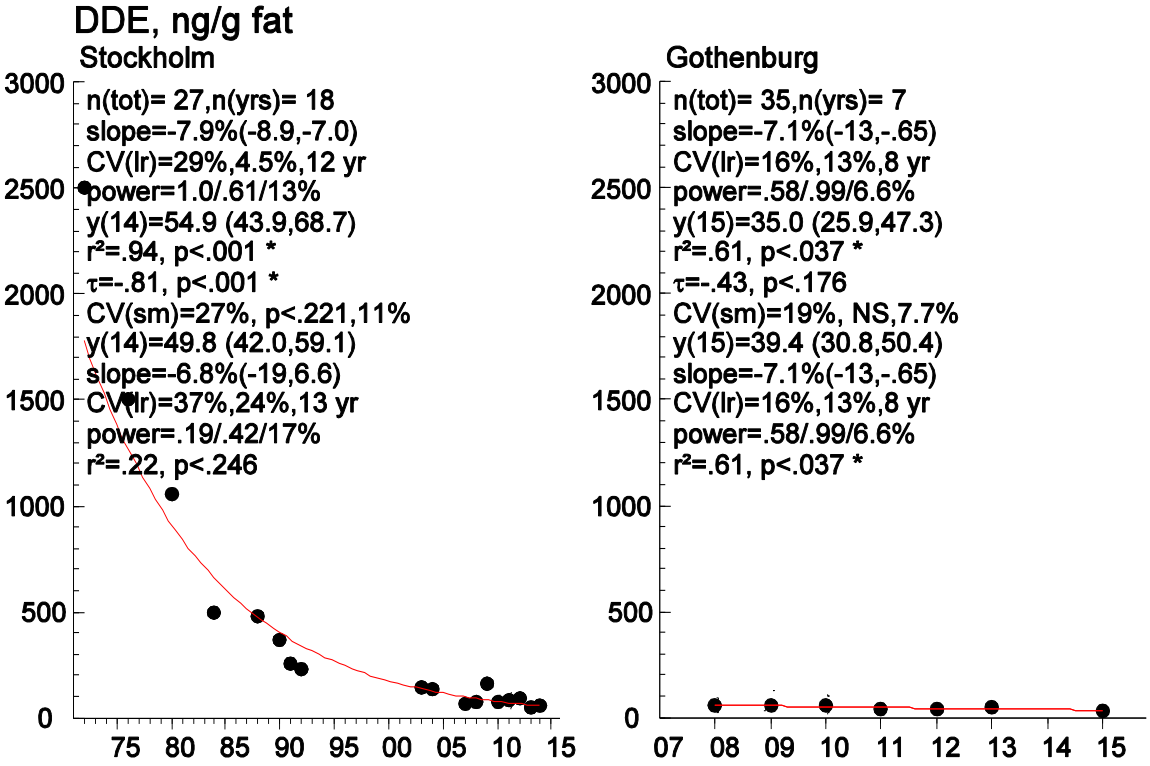

Figure 10.1 Temporal trend of DDE (ng/g fat) in human milk from Stockholm (1972-2014) and Gothenburg (2008-2015).

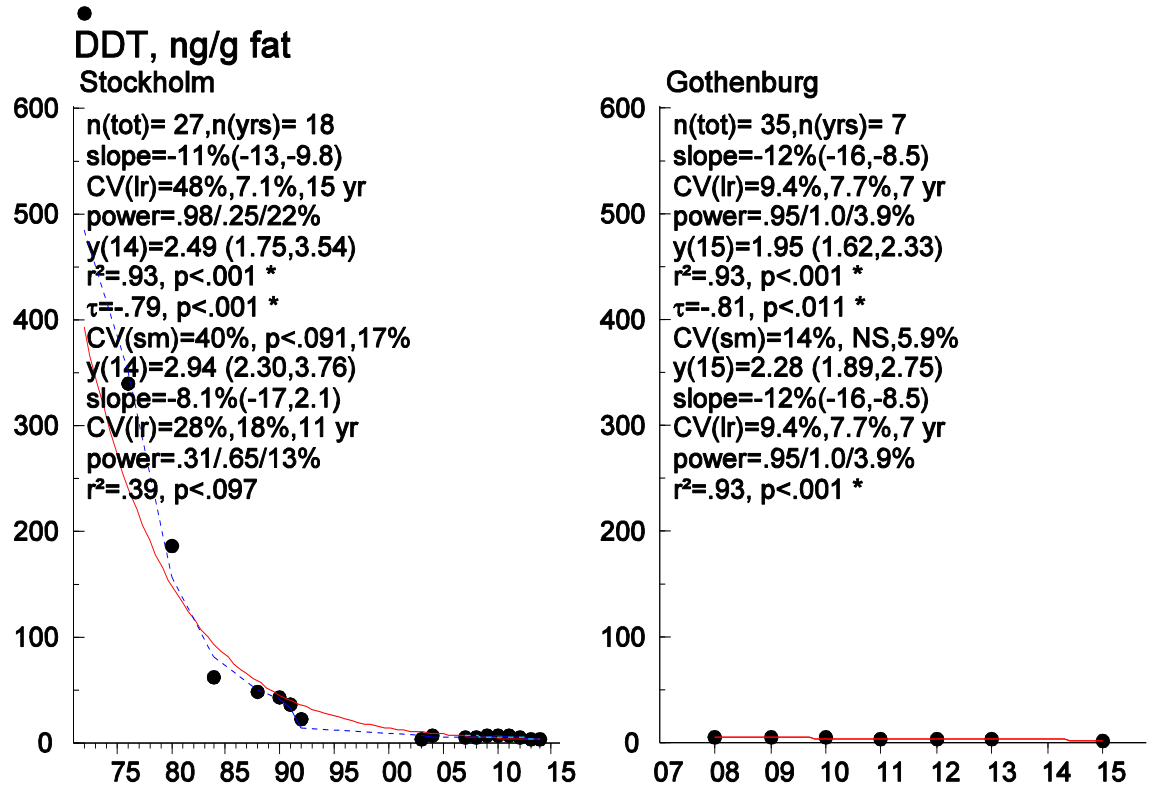

Figure 10.2 Temporal trend of DDT (ng/g fat) in human milk from Stockholm (1972-2014) and Gothenburg (2008-2015).

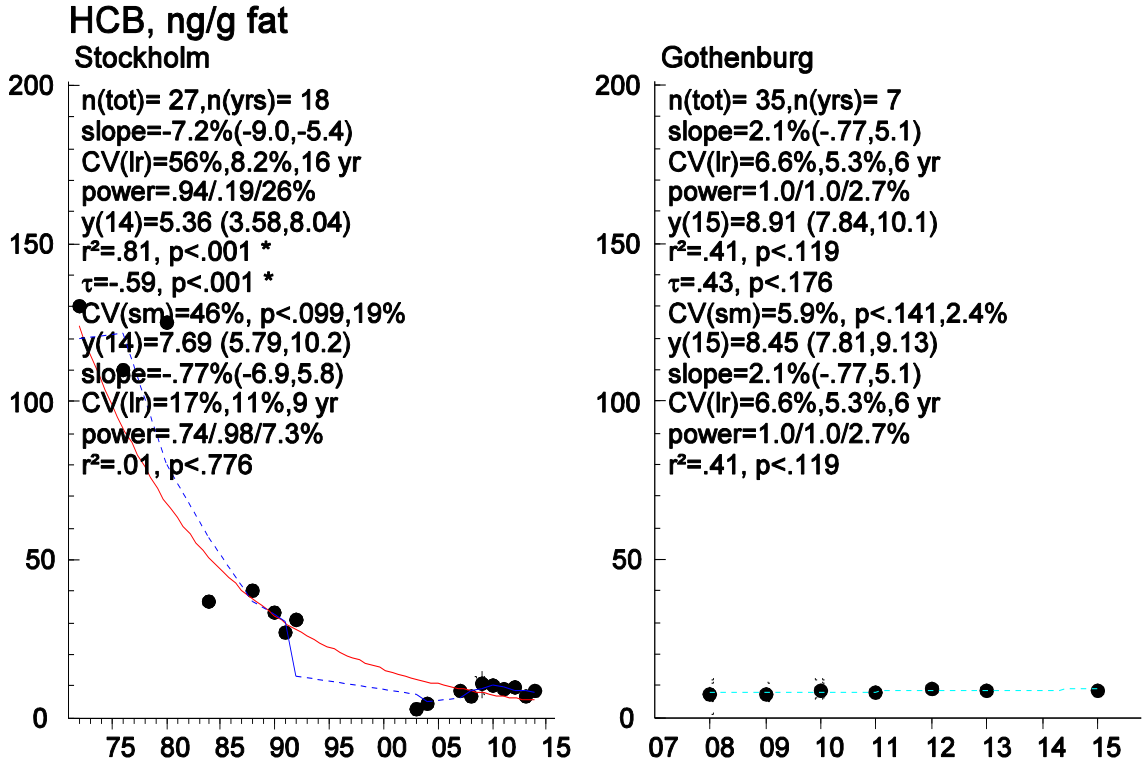

Figure 10.3 Temporal trend of HCB (ng/g fat) in human milk from Stockholm (1972-2014) and Gothenburg (2008-2015).

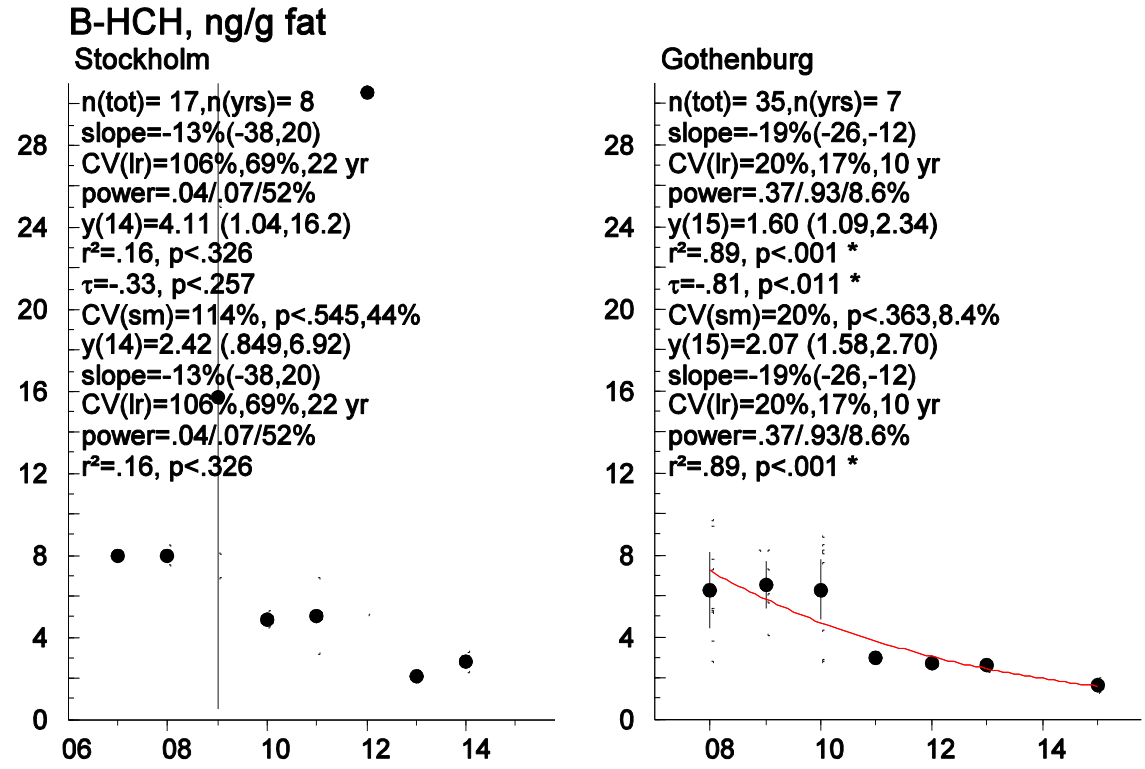

Figure 10.4 Temporal trend of β-HCH (ng/g fat) in human milk from Stockholm (2007-2014) and Gothenburg (2008-2015).

10.2.2 Concentrations and spatial differences

The concentration of DDE in 2014/2015 estimated from the smoothed line was in Stockholm (50 ng/g fat) and in Gothenburg (39 ng/g fat) (Table 10.1). These concentrations were in the lower end compared to concentrations reported for other European countries (25-250 ng/g fat) in a review by Fång et al. 2015. Levels of DDE in human milk from some of the countries from the Eastern part of Europe were much higher, 250-2800 ng/g fat (Fång et al. 2015). Lignell et al. 2014 reported a mean concentration of 39 ng/g fat for DDE in human milk from Uppsala (2012), which was in good agreement with the concentrations reported here.

The concentration of HCB in 2014/2015 was in Stockholm (7.7 ng/g fat) and in Gothenburg (8.5 ng/g fat) (Table 10.1). These concentrations were lower than concentrations reported for other European countries (in general between 10-100 ng/g fat) by Fång et al. 2015. Only two European studies in Fång et al. 2015 reported mean concentrations of HCB below 10 ng/g fat. Lignell et al. 2014 reported a mean concentration of 7.2 ng/g fat for HCB in human milk from Uppsala (2012), which was in line with concentrations reported here.

The concentration of β-HCH in 2014/2015 estimated from the smoothed line was in Stockholm (2.4 ng/g fat) and in Gothenburg (2.1 ng/g fat) (Table 10.1). There were two exeptionally high values in Stockholm in 2009 (25 ng/g fat) and 2012 (56 ng/g fat). The sample from 2012 has been reanalysed but no error could be detected in the chemical analysis. Neither could it be explained by the fat content in the sample. The concentrations of ∑HCHs (where the major part consists of β-HCH) reported for other European countries (10-100 ng/g fat) in Fång et al. 2015 were higher than the concentrations reported here. Lignell et al. 2014 reported a mean concentration of 2.8 ng/g fat for β-HCH in human milk from Uppsala (2012), which was in line with the concentrations reported here.

The PCA (Figure 10.5) show a tendency of higher relative average concentrations of HCB in Gothenburg and higher relative average concentrations of DDE and β-HCH in Stockholm, but there was no significant difference in the DDE, DDT, HCB and β-HCH pattern between Stockholm and Gothenburg (2011-2015).

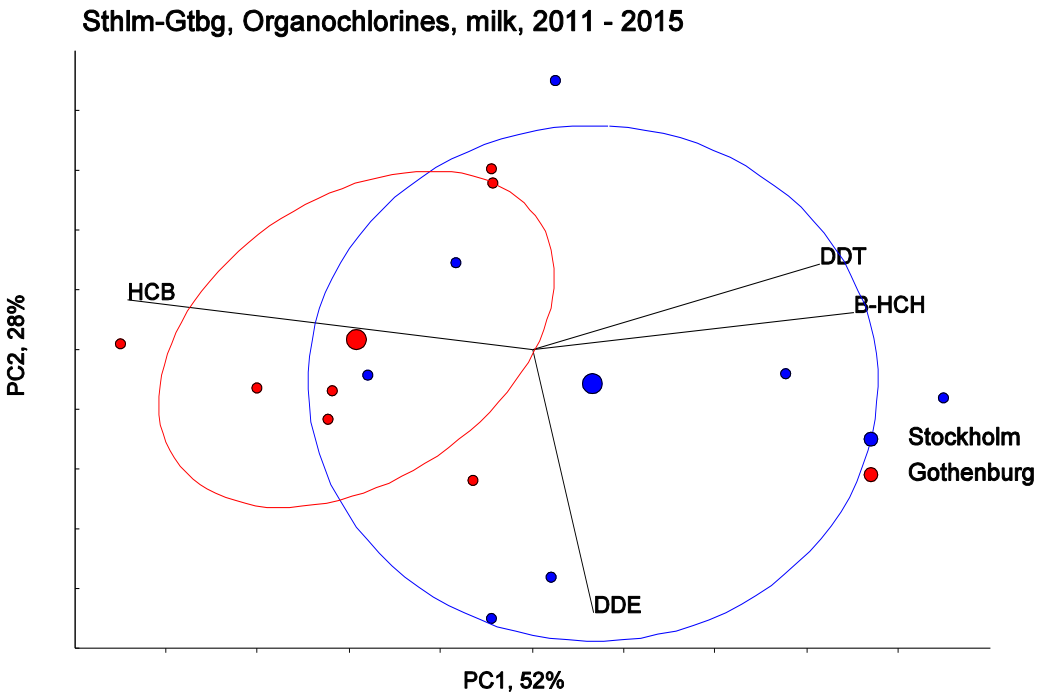

Figure 10.5 PCA (principal component analysis), biplot and Hotellings 95 % confidence ellipses for center of gravity for each group. The figure shows the DDE, DDT, HCB and β-HCH in human milk from Stockholm and Gothenburg (2011-2015). A high (10 times) value for β-HCH 2012 was excluded from the PCA.

10.3 Conclusion

The concentrations of DDE, DDT and HCB in human milk from Stockholm decreased significantly during the whole monitoring period and so did DDE and DDT in the milk from Gothenburg during the most recent ten years. The concentrations reported here were comparable to concentrations reported from other countries in Europe, but for the majority of the substances the concentrations were in the lower end. There was no significant difference in the pattern for DDE, DDT, HCB and β-HCH between Stockholm and Gothenburg.

11 Polychlorinated Dioxins, Dibenzofurans and Dioxinlike Polychlorinated Biphenyls

11.1 Introduction

Polychlorinated dibenzo-p-dioxins (PCDD) and dibenzofurans (PCDF) are formed in several industrial processes and from most combustion processes (e.g., municipal waste incineration and small scale burning in poorly controlled conditions). The use of chlorine gas during pulp bleaching processes was formerly an important source of PCDD/Fs.
PCBs are described in more detail in Chapter 9.

11.2 Results

In this study the **PCDDs**; 2,3,7,8-TCDD, 1,2,3,7,8-PeCDD, 1,2,3,4,7,8-HxCDD, 1,2,3,6,7,8-HxCDD, 1,2,3,7,8,9-HxCDD, 1,2,3,4,6,7,8-HpCDD, OCDD, the **PCDFs**; 2,3,7,8-TCDF, 1,2,3,7,8-PeCDF, 2,3,4,7,8-PeCDF, 1,2,3,4,7,8-HxCDF, 1,2,3,6,7,8-HxCDF, 1,2,3,7,8,9-HxCDF, 2,3,4,6,7,8-HxCDF, 1,2,3,4,6,7,8-HpCDF, 1,2,3,4,7,8,9-HpCDF, OCDF and the dioxin-like PCBs (**dl-PCBs)**; CB-77, CB-81, CB-105, CB114, CB-118, CB-123, CB-126, CB-156, CB-157, CB-167, CB-169 and CB-189 were analysed. The groups are presented as ∑PCDDs, ∑PCDFs, ∑dl-PCBs and ∑PCDDs+PCDFs+dl-PCBs (∑TEQ) in $TEQ_{(WHO\text{-}2005)}$ concentrations in the table and figures. For CB-77 all results were below LOQ. Additional data from Fång et al. 2013, was also included in the temporal trend analysis.

Table 11.1 Trend for the entire period (and the last 10 year period for Stockholm) (in %) for **∑PCDDs, ∑PCDFs, ∑dl-PCBs and ∑PCDDs+PCDFs+dl-PCBs (∑TEQ)** assessed from the annual means ($TEQ_{(WHO\text{-}2005)}$ pg/g fat) in human milk from Stockholm and Gothenburg. P shows the p-value, YRQ: years required to detect an annual change of 10 % with a power of 80 % and LDT: lowest detectable trend (given in percent per year) for a ten year period with the current between-year variation at a power of 80 %. Last year's concentration is estimated from the smoothed trend. Numbers in brackets are 95 % confidence intervals (C.I.). The total number of samples and the number of years for the various time-series are shown in columns two and three.

Substance	Sampling site	N samples	N years	Period (Years)	Trend % (95 % C.I.)	P	YRQ	LDT %	Last year pg/g l.w. (95 % C.I.)
∑PCDDs	Stockholm	35	25	72-14	-5.9(-6.6,5.1)	**0.001**	11	11	1.89(1.77,2.02)
	Stockholm		8	07-14	-1.4(-6.5,4.0)	0.539	8	6.0	
	Gothenburg	14	8	07-15	-7.8(-10,-5.2)	**0.001**	6	3.3	1.49(1.35,1.63)
∑PCDFs	Stockholm	35	25	72-14	-5.6(-6.1,-5.1)	**0.001**	8	6.4	1.36(1.27,1,46)
	Stockholm		8	07-14	.93(-5.7,8.0)	0.751	9	7.8	
	Gothenburg	14	8	07-15	-5.5(-7.91,-3.1)	**0.001**	6	3.0	1.12(1.05,1.20)
∑dl-PCBs	Stockholm	35	25	72-14	-6.5(-7.2,-5.9)	**0.001**	10	9.7	2.07(1.86,2.31)
	Stockholm		8	07-14	-3.3(-15,9.3)	0.523	13	15	
	Gothenburg	14	8	07-15	-7.7(-9.8,-5.6)	**0.001**	6	2.7	2.04(1.86,2.24)
∑TEQ	Stockholm	35	25	72-14	-6.1(-6.7,-5.6)	**0.001**	9	7.7	5.32(4.97,5.70)
	Stockholm		8	07-14	-1.9(-9.6,6.4)	0.87	10	9.5	
	Gothenburg	14	8	07-15	-7.1(-8.7,5.4)	**0.001**	5	2.1	4.68(4.38,5.00)

11.2.1 Temporal variation

The concentrations of ∑PCDDs, ∑PCDFs, ∑dl-PCBs and ∑PCDDs+PCDFs+dl-PCBs in human milk from Stockholm decreased significantly during the time period 1972–2014 (Figure 11.1, 11.2, 11.3, 11.4 and Table 11.1), with an annual mean decrease of -5.6 to -6.5 %. Similarly significant downward trends were also observed in human milk from Gothenburg of -5.5 to -7.8 % per year (2007-2015) (Figure 11.1, 11.2, 11.3, 11.4 and Table 11.1). In contrast no significant downward trends were observed in human milk from Stockholm during the most recent ten year period, instead the concentrations seem to have levelled out. The ability to detect trends in Stockholm during the most recent ten year period might however been affected by the change of analytical laboratory in 2012.

The temporal trend for ∑PCDDs, ∑PCDFs and ∑PCDDs+PCDFs+dl-PCBs in human milk reported in this study was of similar magnitude as the temporal trends reported by Lignell et al. 2014 (Uppsala, 1996-2012), which showed significant downward trends of -6.8, -4.9 and -6.8 % per year, respectively. The trends for PCDDs and PCDFs in human milk from Stockholm were comparable to the trends seen in Swedish marine (Bignert et al. 2017) and freshwater (Nyberg et al. 2016) biota where concentrations decreased significantly in the beginning of the monitoring period, but then levelled out during more recent years.

The number of years required to detect an annual change of 10 % for ∑PCDDs, ∑PCDFs, ∑dl-PCBs and ∑PCDDs+PCDFs+dl-PCBs varied between 6-13 years.

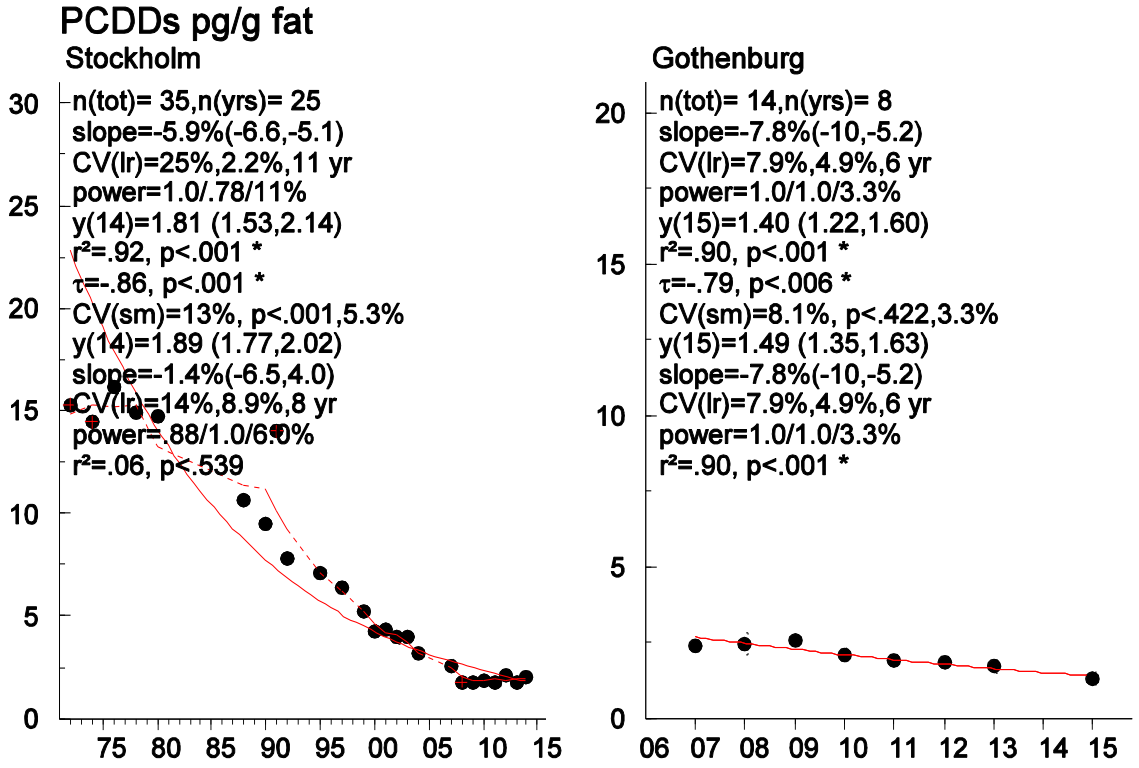

Figure 11.1 Temporal trend of ∑PCDDs (TEQ $_{(WHO-2005)}$ pg/g fat) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015).

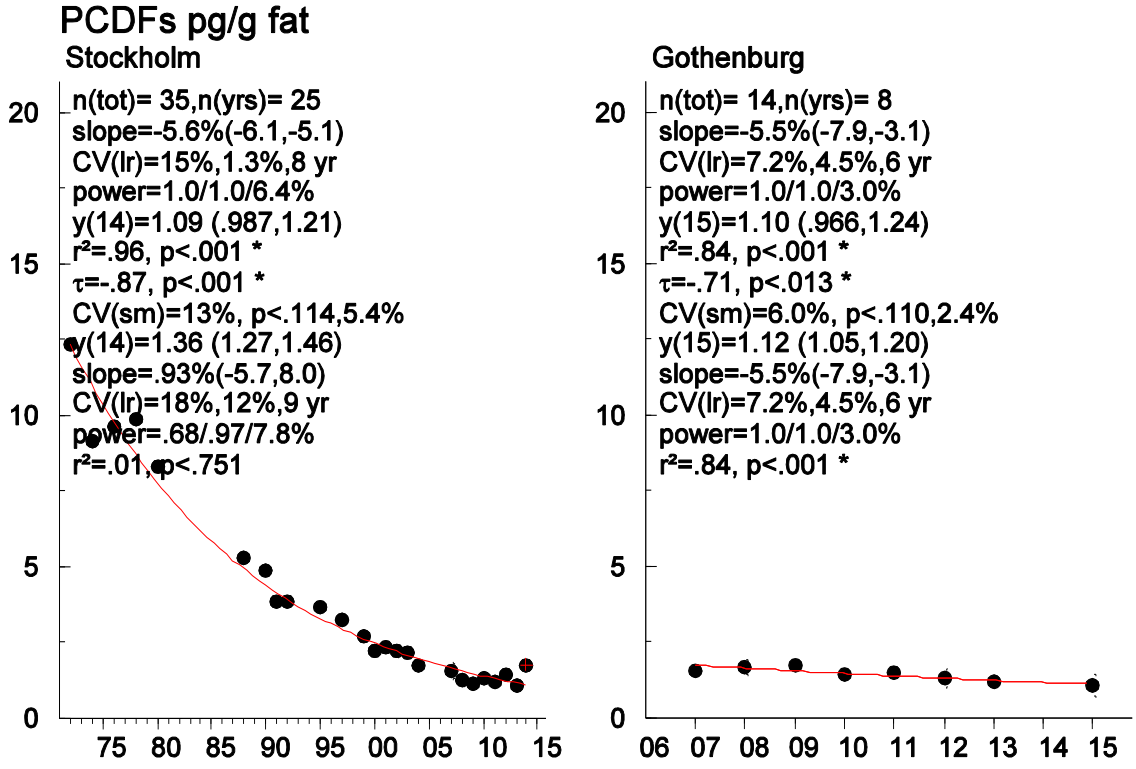

Figure 11.2 Temporal trend of ∑PCDFs (TEQ $_{(WHO-2005)}$ pg/g fat) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015).

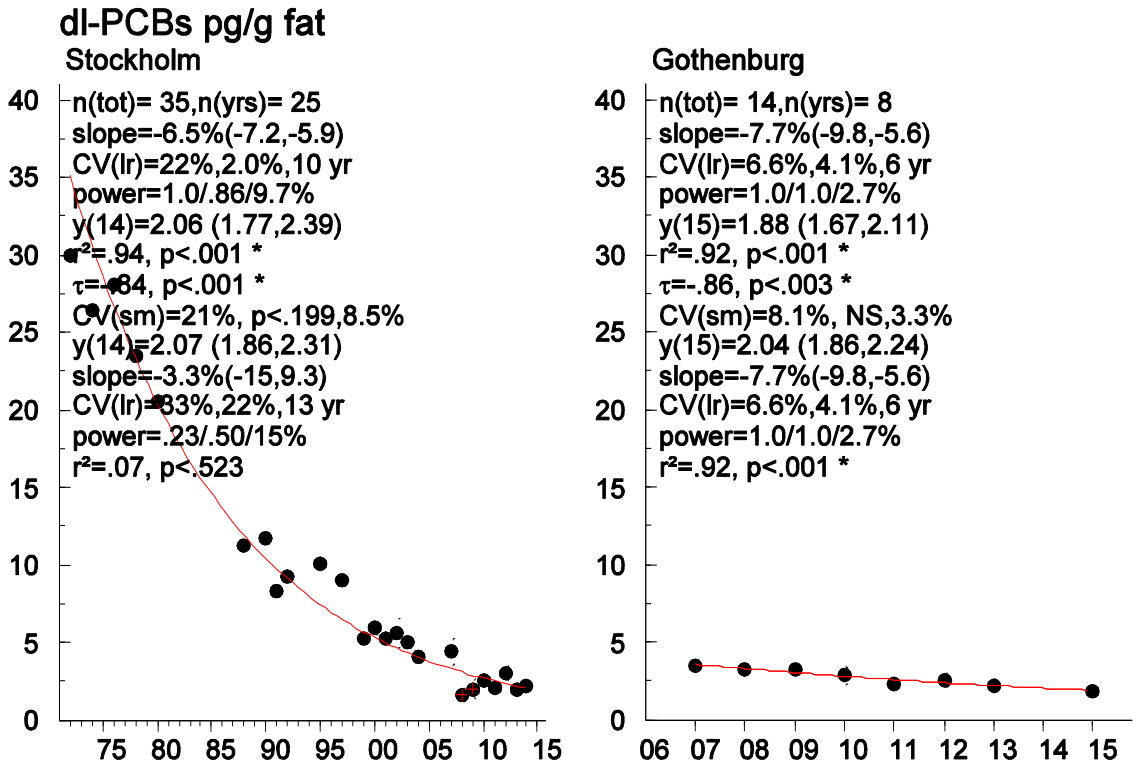

Figure 11.3 Temporal trend of ∑dl-PCBs (TEQ $_{(WHO-2005)}$ pg/g fat) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015).

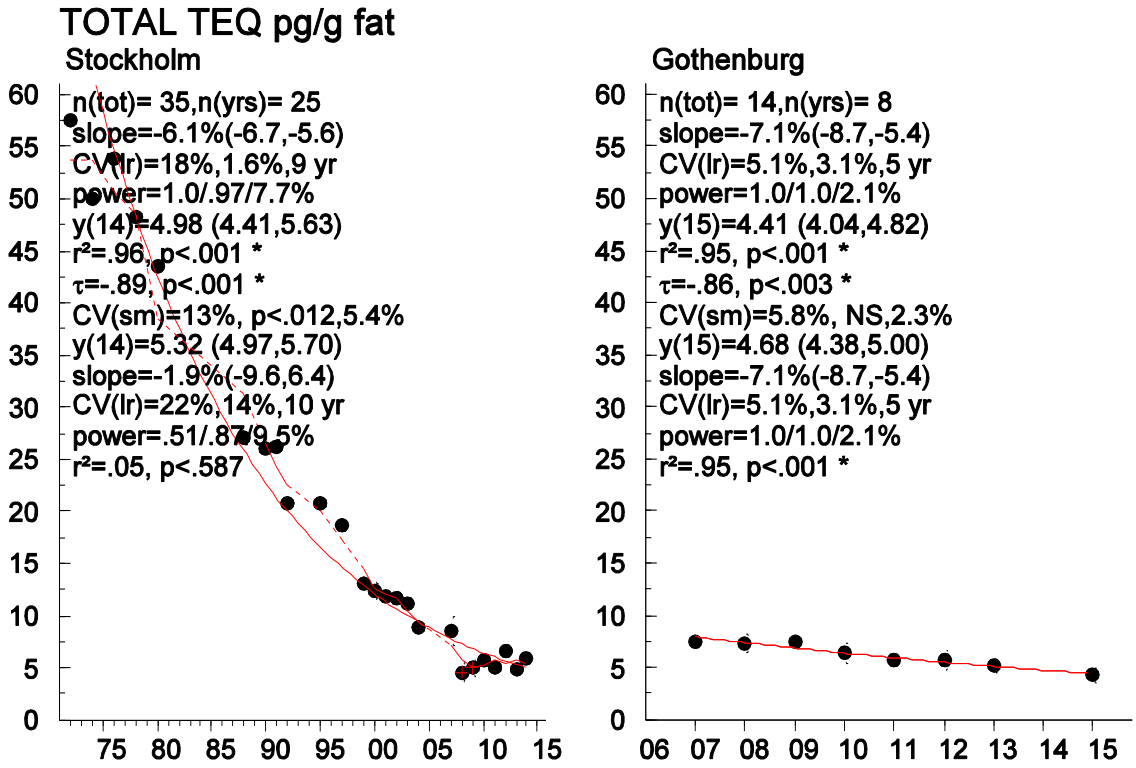

Figure 11.4 Temporal trend of ∑PCDDs+PCDFs+dl-PCBs (TOTAL TEQ) (TEQ $_{(WHO\text{-}2005)}$ pg/g fat) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015).

11.2.2 Concentrations and spatial differences

The concentration of ∑PCDDs+PCDFs+dl-PCBs in 2014/2015 estimated from the smoothed line was in Stockholm (5.3 TEQ $_{(WHO\text{-}2005)}$ pg/g fat) and in Gothenburg (4.7 TEQ $_{(WHO\text{-}2005)}$ pg/g fat). These concentrations were in the lower end compared to concentrations reported for other European countries (2.9-31 TEQ $_{(WHO\text{-}2005)}$ pg/g fat)) in a review by Fång et al. 2015. The concentrations reported from European countries in Fång et al. 2015 were higher compared to countries in Africa and South America. Lignell et al. 2014 reported mean concentrations of 1.9, 1.3 and 5.7 TEQ $_{(WHO\text{-}2005)}$ pg/g fat for ∑PCDDs, ∑PCDFs and ∑PCDDs+PCDFs+dl-PCBs in human milk from Uppsala (2012), which was in good agreement with the concentrations reported here.

The PCA (Figure 11.5) show no significant difference in the ∑PCDDs, ∑PCDFs and ∑dl-PCBs pattern between Stockholm and Gothenburg (2012-2015).

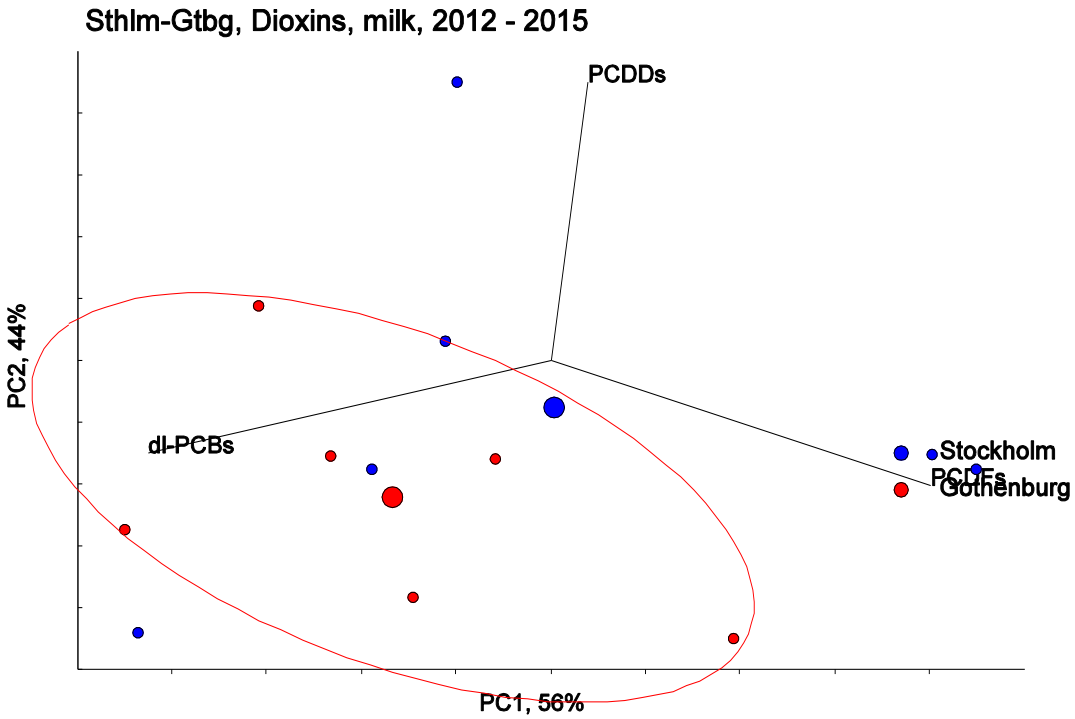

Figure 11.5. PCA (Principal Component Analysis), biplot and Hotellings 95 % confidence ellipses for center of gravity for each group. The figure shows the ∑PCDDs, ∑PCDFs, ∑dl-PCBs in human milk from Stockholm and Gothenburg (2012-2015).

11.3 Conclusion

The concentrations of ∑PCDDs, ∑PCDFs, ∑dl-PCBs and ∑PCDDs+PCDFs+dl-PCBs in human milk from Stockholm and Gothenburg decreased significantly during the whole monitoring period. However during the most recent ten year period no trends were observed for the Stockholm milk. The concentrations reported here were comparable to concentrations reported from other countries in Europe although in the lower end. There was no significant difference in the pattern for ∑PCDDs, ∑PCDFs, ∑dl-PCBs between Stockholm and Gothenburg.

12 Brominated flame retardants

12.1 Introduction

Polybrominated diphenyl ethers (PBDEs) are produced as three different technical products; penta-, octa- and decabromo diphenyl ether (BDE). Each of these products includes a few major congeners. For pentaBDE these are BDE-47, -99, and -100. OctaBDE contains mainly BDE-183, while decaBDE includes almost exclusively BDE-209 (La Guardia et al. 2006). Hexabromocyclododecan (HBCDD) is produced as a mixture of three stereoisomers – α-, β- and γ-HBCDD (Covaci A. et al. 2006). Both PBDEs and HBCDD are used as additive flame retardants incorporated into materials such as plastics and textiles. DBE-DBCH is an emerging flame retardant and consists of the stereoisomers α- and β- DBE-DBCH. DBE-DBCH is used in polystyrene insulation, wire coating, high-impact appliance plastic, and fabric adhesives (Marteinson et al. 2015).

PBDEs and HBCDD leak into the environment during production, use, or disposal of such products and are mainly spread via diffuse distribution in the atmosphere and in rivers. They are bioaccumulative, lipophilic and persistent, and accumulate in the food-web. In a doctoral thesis by Newton (2015), it is indicated that DBE-DBCH behaves in a similar manner as PBDEs in the environment.

More comprehensive information concerning PBDEs and HBCDD, e.g. sources and environmental fate, can be found in the extensive reports from the European Food Safety Authority (EFSA), on PBDEs (EFSA, 2012) and HBCDD (EFSA, 2011).

12.2 Results

The BFRs analysed within this study from Stockholm (2010-2014) and Gothenburg (2011-2015) were BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, BDE-154, BDE-209, HBCDD α- and β- DBE-DBCH. For BDE-154, α- and β- DBE-DBCH all measurements were below LOQ. For BDE-209 all measurements were below LOQ except two, from Gothenburg 2012 and 2015, where the concentrations were 1.4 and 0.94 ng/g fat, respectively. For BDE-28 and HBCDD, about 50 % of the measurements, were below LOQ (LOQ ranged between 0.04 and 0.1 ng/g fat). The concentrations of BDE-47, BDE-100 and BDE-153 reported for the two samples from Stockholm 2013 were suspiciously high. It is possible that some kind of contamination has occurred and further investigations are needed. Additional data for BDE-47, BDE-99, BDE-100 and HBCDD from Athanasiadou and Bergman 2008, Fängström et al 2008 and Bergman et al. 2010, were also included in the temporal trend analysis.

Table 12.1 Trend for the entire period (and the last 10 year period in Stockholm) (in %) for **BDE-28**, **BDE-47**, **BDE-99**, **BDE-100**, **BDE-153** and **HBCDD** assessed from the annual means (ng/g fat) in human milk from Stockholm and Gothenburg. P shows the p-value, YRQ: years required to detect an annual change of 10 % with a power of 80 % and LDT: lowest detectable trend (given in percent per year) for a ten year period with the current between-year variation at a power of 80 %. Last year's concentration is estimated from the smoothed trend. Numbers in brackets are 95 % confidence intervals (C.I.). The total number of samples and the number of years for the various time-series are shown in columns two and three.

Substance	Sampling site	N samples	N years	Period (Years)	Trend % (95 % C.I.)	P	YRQ	LDT %	Last year ng/g l.w. (95 % C.I.)
BDE-28	Stockholm	15	7	07-14	-14(-32,9.0)	0.164	17	29	0.081(0.034,0.193)
	Gothenburg	19	6	07-15	-11(-18,-3.6)	**0.016**	10	8.7	0.056(0.039,0.079)
BDE-47	Stockholm	33	21	84-14	1.8(-1.3,5.0)	0.234	18	30	1.75(1.44,2.13)
	Stockholm		8	07-14	4.7(-13,25)	0.555	16	24	
	Gothenburg	38	8	07-15	-21(-29,-13)	**0.001**	12	13	0.282(0.200,0.397)
BDE-99	Stockholm	26	20	84-14	-.77(-4.7,3.3)	0.689	20	41	0.345(0.277,0.431)
	Stockholm		8	07-14	9.5(-3.3,24)	0.119	12	14	
	Gothenburg	38	8	07-15	-18(-29,-6.5)	**0.010**	14	18	0.058(0.041,0.083)
BDE-100	Stockholm	23	18	84-14	2.7(-.47,5.9)	0.091	17	28	0.594(0.438,0.805)
	Stockholm		8	07-14	20(-46,164)	0.525	21	45	
	Gothenburg	38	8	07-15	-18(-26,-9.3)	**0.003**	12	13	0.083(0.058,0.123)
BDE-153	Stockholm	13	7	07-14	16(-17,63)	0.302	22	48	1.81(0.517,6.30)
	Gothenburg	38	8	07-15	-1.7-6.7,3.6)	0.458	8	6.4	0.458(0.385,0.544)
HBCDD	Stockholm	23	18	84-14	.056(-3.7,4.0)	0.978	19	37	0.156(0.097,0.250)
	Stockholm		8	07-14	.56(-68,212)	0.969	26	77	
	Gothenburg	7	4	11-15	-48(-82,48)	0.1171	20	40	.033(.001,.551)

12.2.1 Temporal variation

The concentrations of BDE-47, BDE-99 and BDE-100 decreased significantly in human milk from Gothenburg (2007-2015) (Figure 12.2, 12.3, 12.4 and Table 12.1), with an annual mean decrease of -18 to -21 %. Downward trends were also indicated for BDE-28 and HBCDD in Gothenburg. In contrast, no trend was detected for the PBDEs and HBCDD, neither during the whole monitoring period nor during the most recent ten year period, in human milk from Stockholm (Figure 12.1, 12.2, 12.3, 12.4, 12.5 and Table 12.1). However, the concentrations of BDE-47, BDE-100 and BDE-153 measured in the samples from 2013 in Stockholm were high compared to the rest of the concentrations, which affect the ability to detect trends during the most recent ten years in the milk from Stockholm. The change in analytical laboratory in 2010 might also affect the ability to detect trends. The comparison between the two analytical methods indicated that the concentrations measured in the present study were slightly higher than in Bergman et al. 2010 (more information in Chapter 5).

The decreasing concentrations for BDE-47, BDE-99 and BDE-100 in human milk from Gothenburg reported in the present study are of similar magnitude (or decreasing at a slightly faster rate) as the temporal trends reported by Lignell et al. 2014 (Uppsala, 1996-2012), which showed significant downward trends of -8.6, 10 and 4.8 % per year, respectively.

The number of years required to detect an annual change of 10 % for BDE-28, BDE-47, BDE-99, BDE-100, BDE-153 and HBCDD varied between 8-26 years.

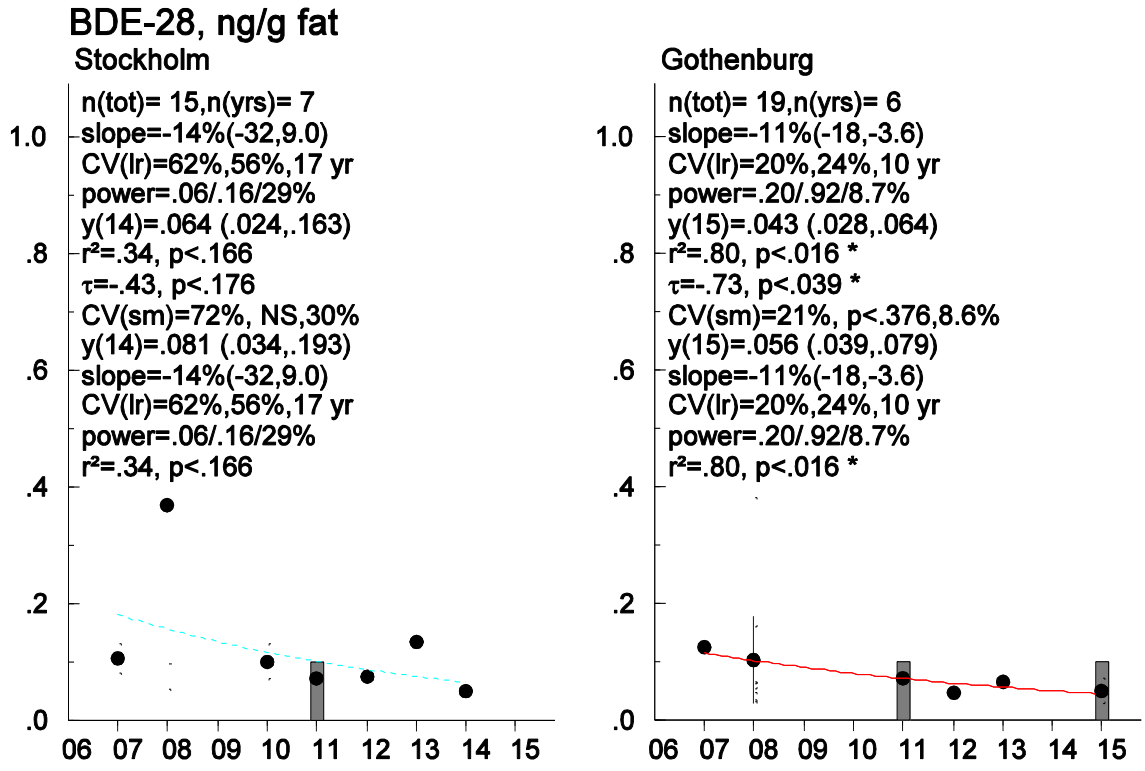

Figure 12.1 Temporal trend of BDE-28 (ng/g fat) in human milk from Stockholm (2007-2014) and Gothenburg (2007-2015). The grey bars represent years where all values are below LOQ.

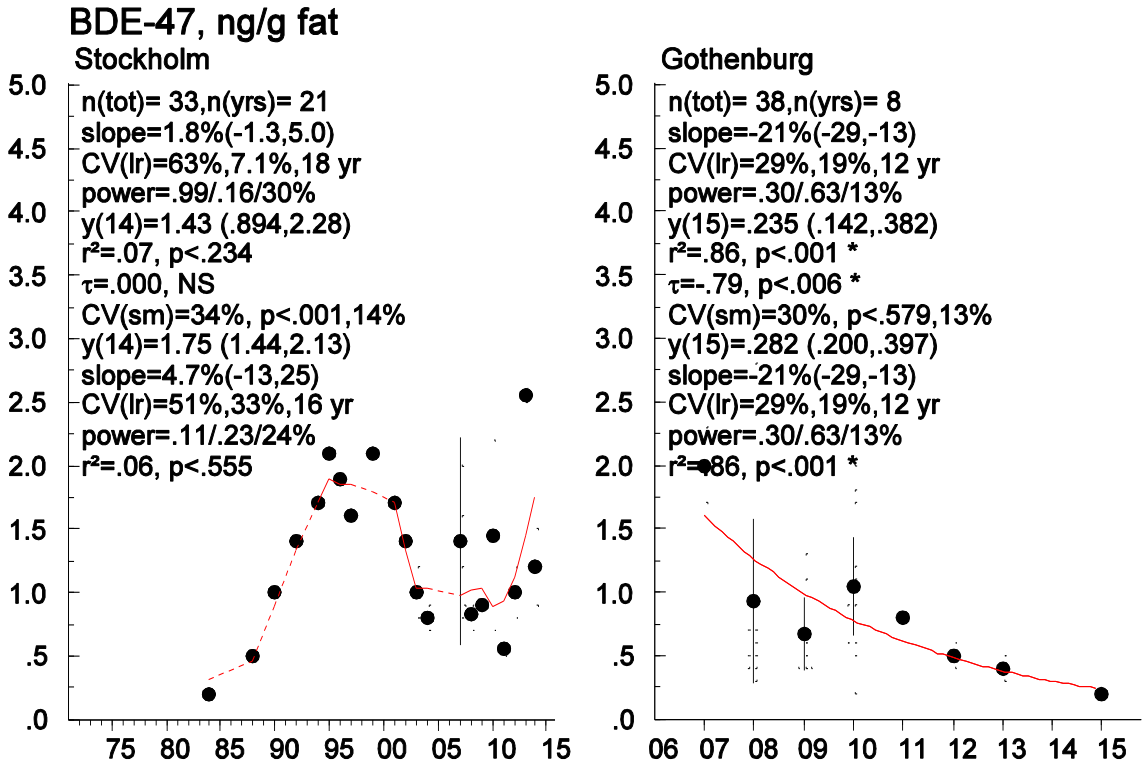

Figure 12.2 Temporal trend of BDE-47 (ng/g fat) in human milk from Stockholm (1984-2014) and Gothenburg (2007-2015).

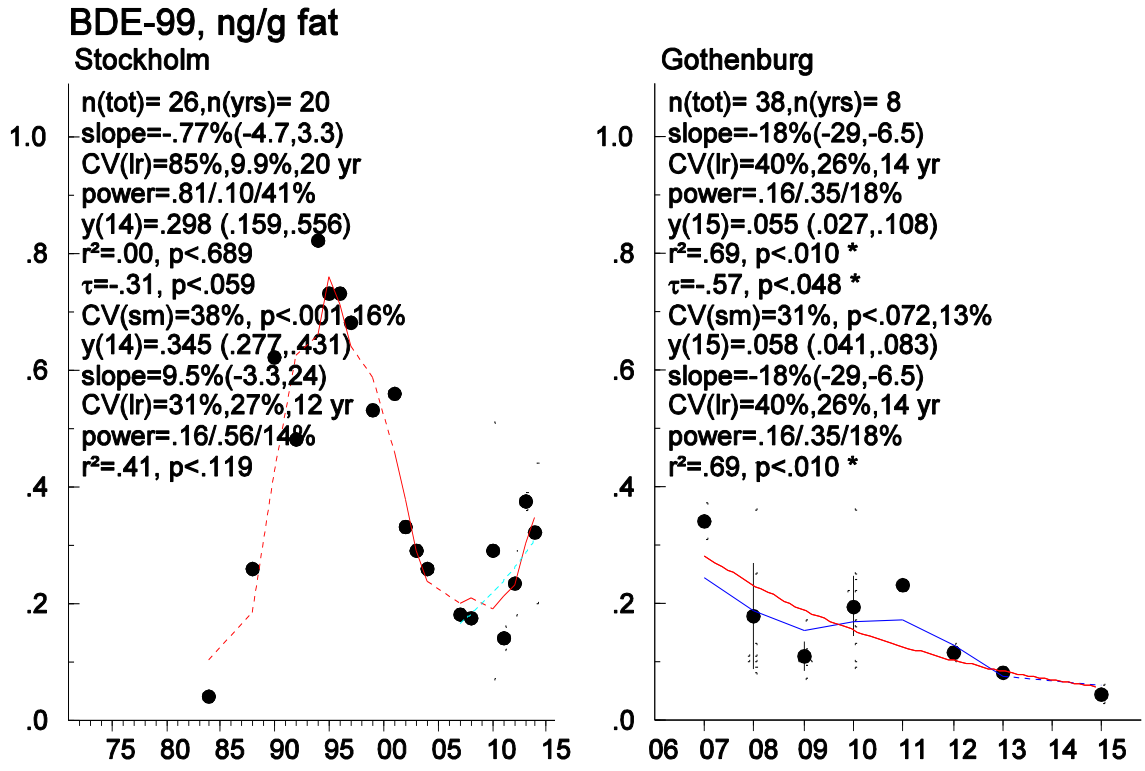

Figure 12.3 Temporal trend of BDE-99 (ng/g fat) in human milk from Stockholm (1984-2014) and Gothenburg (2007-2015).

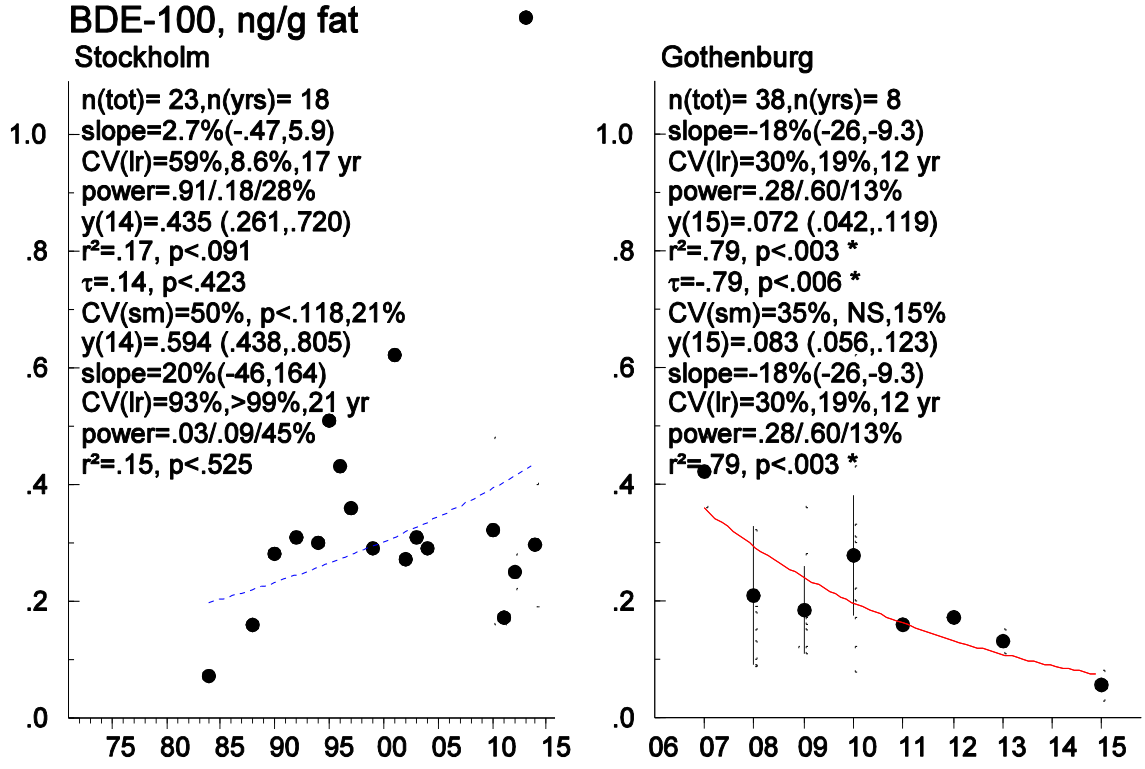

Figure 12.4 Temporal trend of BDE-100 (ng/g fat) in human milk from Stockholm (1984-2014) and Gothenburg (2007-2015).

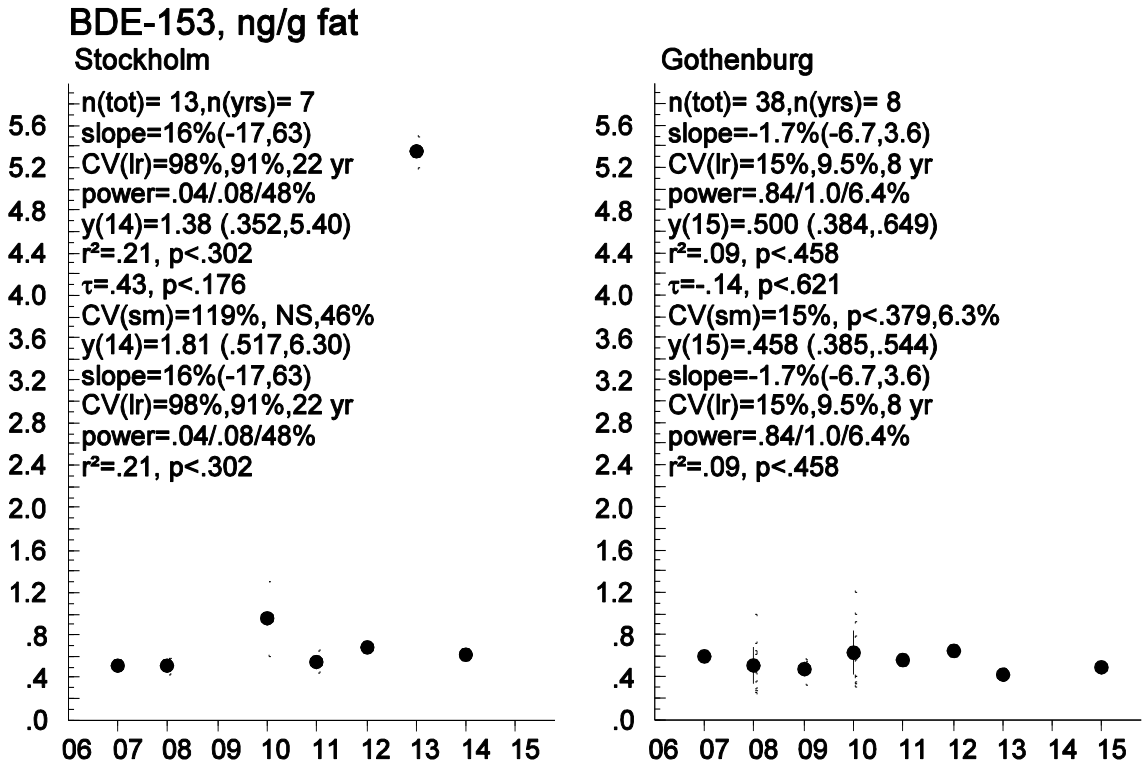

Figure 12.5 Temporal trend of BDE-153 (ng/g fat) in human milk from Stockholm (1984-2014) and Gothenburg (2007-2015).

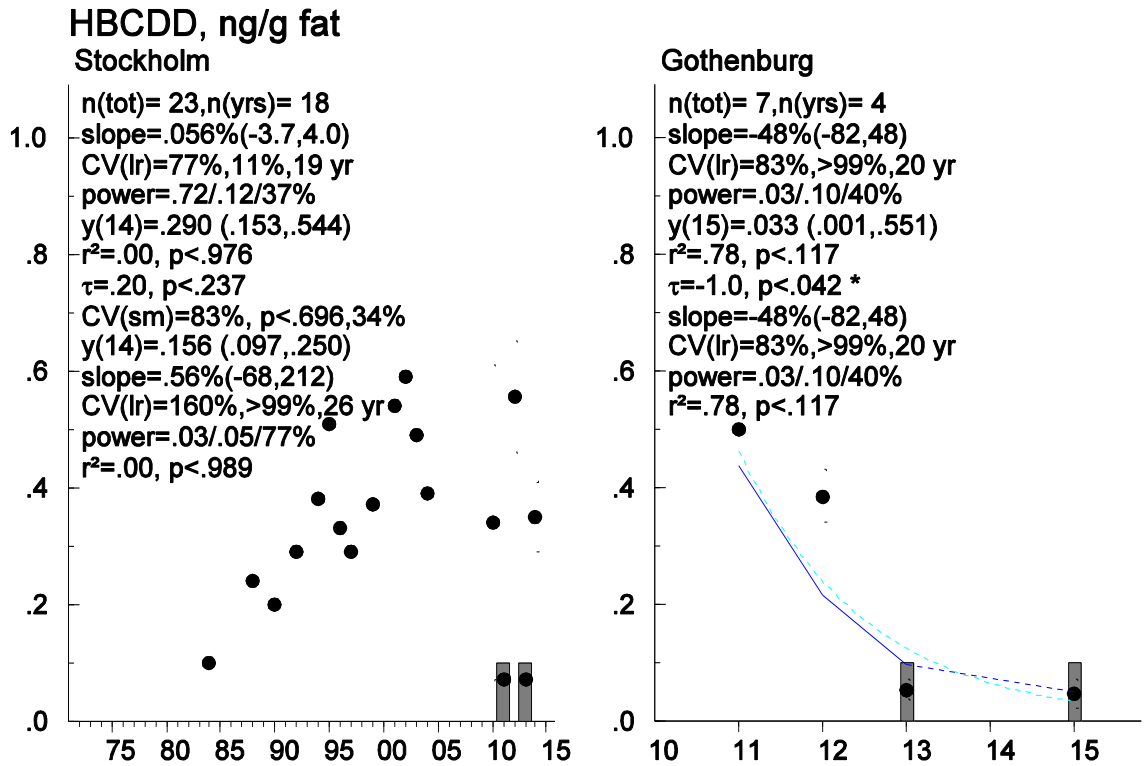

Figure 12.5 Temporal trend of HBCDD (ng/g fat) in human milk from Stockholm (1984-2014) and Gothenburg (2011-2015). The grey bars represent years where all values are below LOQ.

12.2.2 Concentrations and spatial differences

The concentration of BDE-47 in 2014/2015 estimated from the smoothed line was in Stockholm (1.8 ng/g fat) and in Gothenburg (.28 ng/g fat). The difference in concentration between the two cities could, at least partly, be explained by the two exceptionally high values in Stockholm in 2013 (2.6 and 2.5 ng/g fat). The concentrations of BDE-47 reported from other countries in Europe were approximately 1-2 ng/g fat (Fång et al. 2015), which is similar to the concentration reported from Stockholm, but higher than in human milk from Gothenburg. Lignell et al. 2014 reported a mean concentration of 0.84 ng/g fat for BDE-47 in human milk from Uppsala (2012), which was in between the concentrations reported here. The concentrations of BDE-153, BDE-100, BDE-99 and BDE-28 reported in the Uppsala study were slightly higher than the concentrations in the milk from Gothenburg, but lower than in the milk from Stockholm.

The concentration of HBCDD in 2014/2015 estimated from the smoothed line was in Stockholm (0.16 ng/g fat) and in Gothenburg (.033 ng/g fat). The levels of HBCDD in Europe ranged between 0.33 to 6.0 ng/g fat. The highest concentrations reported were from a Spanish study, with a mean concentration of 47 ng/g fat (Fång et al. 2015). The mean concentration in human milk from Uppsala (2012) reported by Lignell et al. 2014 was 0.4 ng/g, which was higher than the concentrations reported here.

The PCA (Figure 12.6) show a tendency of higher relative average concentrations of HBCDD in Gothenburg and higher relative average concentrations of BDE-99 in Stockholm, but there was no significant difference in the BDE-47, BDE-99, BDE-100, BDE-153 and HBCDD pattern between Stockholm and Gothenburg (2011-2015). The high concentrations in 2013 could have a significant effect on the PCA.

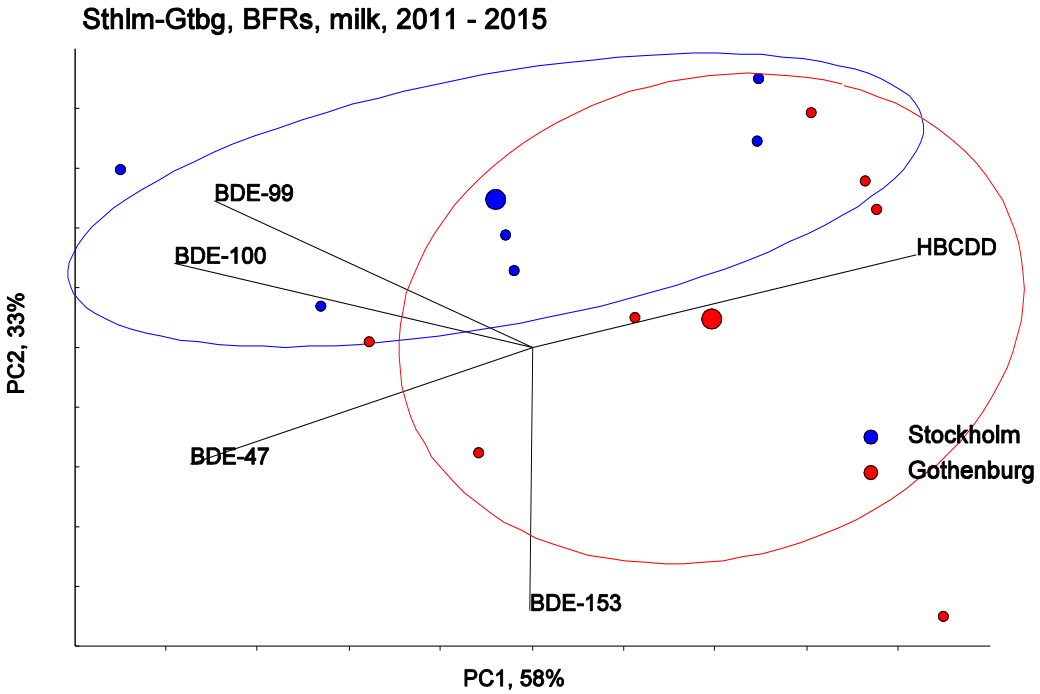

Figure 12.6 PCA (principal component analysis), biplot and Hotellings 95 % confidence ellipses for center of gravity for each group. The figure shows the BDE-47, BDE-99, BDE-100, BDE-153 and HBCDD in human milk from Stockholm and Gothenburg (2011-2015).

12.3 Conclusion

The concentrations of BDE-47, BDE-99 and BDE-100 in human milk from Gothenburg decreased significantly during 2007-2015. No trends were observed in the milk from Stockholm. The concentrations reported here for BDE-47 and HBCDD were comparable to or slightly lower than concentrations reported from other countries in Europe. There was no significant difference in the pattern for BDE-47, BDE-99, BDE-100, BDE-153 and HBCDD between Stockholm and Gothenburg.

13 Per- and polyfluooalkyl substances

13.1 Introduction

Per- and polyfluoroalkyl substances (PFASs) are a diverse group of ~3000 anthropogenic substances that have been manufactured for over six decades. Owing to their stability and amphipathic properties, PFASs have been used in a wide range of commercial processes (e.g., production of fluoropolymers) and consumer products (e.g., water and stain proofing agents and fire-fighting foams (Kissa et al. 2001). In the year 2000 the main producer, 3M, began phasing out production of perfluoroctanoate (PFOA) and perfluorooctane sulfonate (PFOS) (Buck et al. 2011.). In May 2009, the Stockholm Convention on Persistent Organic Pollutants listed perfluorooctane sulfonate (PFOS) and its salts into Annex B to restrict/eliminate their production and usage. PFOS-precursors (i.e. substances that may transform to PFOS) are also included under Annex B. Perfluorooctane sulfonamide (FOSA), N-methylperfluorooctanesulfonamidoacetic acid (N-MeFOSAA) and N-ethylperfluorooctanesulfonamidoacetic acid (N-EtFOSAA) are examples of PFOS-precursors included in the present study. These substances may form from oxidation of N-alkyl substituted perfluorooctane sulfonamido ethanols which have been used historically in consumer-related applications, e.g. paper and packaging protectants, carpets and textiles (Lange et al. 2004), but continue to be manufactured in developing countries.

13.2 Results

In this study we analysed 19 PFASs; perfluoropentanoate (PFPeA), perfluorohexanoate (PFHxA), perfluoroheptanoate (PFHpA), PFOA, perfluorononanoate (PFNA), perfluorodecanoate (PFDA), perfluorundecanoate (PFUnDA), perfluorododecanoate (PFDoDA), perfluorotridecanoate (PFTriDA), perfluorotetradecanoate (PFTeDA), perfluoropentadecanoate (PFPeDA), 3-perfluoroheptyl propanoic acid (FHpPA), perfluorobutane sulfonate (PFBS), perfluorohexane sulfonate (PFHxS), PFOS, perfluorodecane sulfonate (PFDS), perfluorooctanesulfonamide (FOSA), N-MeFOSAA and N- EtFOSAA. PFASs for which most years were under LOQ i.e. PFPeA (LOQ=80 pg/ml), PFPeDA (LOQ=1 pg/ml, highest measured concentration 2.29 pg/ml), FHpPA (LOQ=1 pg/ml, highest measured concentration 10.64 pg/ml), PFDS (LOQ=0.5 pg/ml), MeFOSAA (LOQ=5 pg/ml) and EtFOSAA (LOQ=5 pg/ml) were excluded from the trend analysis.

Table 13.1 Trend for the entire period (and the last 10 year period for Stockholm) (in %) for **FOSA, PFBS, PFDA**, **PFDoDA, PFHpA**, **PFHxA**, **PFHxS, PFNA**, **PFOA**, **PFTeDA, PFOS, PFTriDA and PFUDA** assessed from the annual means (pg/ml) in human milk from Stockholm and Gothenburg. P shows the p-value, YRQ: years required to detect an annual change of 10 % with a power of 80 % and LDT: lowest detectable trend (given in percent per year) for a ten year period with the current between-year variation at a power of 80 %. Last year's concentration is estimated from the smoothed trend. Numbers in brackets are 95 % confidence intervals (C.I.). The total number of samples and the number of years for the various time-series are shown in columns two and three.

Substance	Sampling site	N samples	N years	Period (Years)	Trend % (95 % C.I.)	P	YRQ	LDT %	Last year pg/ml (95 % C.I.)
FOSA	Stockholm	40	16	72-14	-4.5(-8.0,-.85)	**0.020**	24	61	1.54(0.939,2.53)
	Stockholm		8	07-14	-.97(-26,33)	0.938	18	32	
	Gothenburg	27	7	07-15	1.4(-18,26)	0.873	18	30	1.94(1.21,3.12)
PFBS	Stockholm	40	16	72-14	-1.7(-4.2,1.0)	0.201	19	38	1.75(1.22,2.52)
	Stockholm		8	07-14	10(-17,46)	0.410	18	30	
	Gothenburg	27	7	07-15	1.4(-7.1,11)	0.699	10	10	0.706(0.522,0.954)
PFDA	Stockholm	40	16	72-14	3.3(1.7,4.9)	**0.001**	14	19	4.09(3.27,5.13)
	Stockholm		8	07-14	-6.4(-17,5.0)	0.198	10	10	
	Gothenburg	27	7	07-15	8.0(-17,1.7)	0.088	11	12	4.49(2.86,7.04)
PFDoDA	Stockholm	40	16	72-14	.29(-.77,1.4)	0.569	11	12	0.706(0.584,0.853)
	Stockholm		8	07-14	-3.3(-20,16)	0.660	14	18	
	Gothenburg	27	7	07-15	-8.6(-15,1.6)	**0.026**	10	8.6	0.706(0.522,0.956)
PFHpA	Stockholm	40	16	72-14	-.12(-1.2,-.97)	0.815	12	13	7.07(5.78,8.64)
	Stockholm		8	07-14	-.72(-7.7,6.8)	0.811	8	6.5	
	Gothenburg	27	7	07-15	-4.5(-12,3.9)	0.219	10	10	7.78(6.01,10.1)
PFHxA	Stockholm	40	16	72-14	-.23(-2.5,2.1)	0.832	18	32	43.0(29.2,63.5)
	Stockholm		8	07-14	15(-8.4,45)	0.174	15	23	
	Gothenburg	27	7	07-15	-3.3(-19,16)	0.650	16	23	23.0(11.6,45.7)
PFHxS	Stockholm	40	16	72-14	3.9(1.3,6.6)	**0.006**	19	35	6.97(4.95,9.81)
	Stockholm		8	07-14	-6.4(-14,1.3)	0.085	9	7	
	Gothenburg	27	7	07-15	-9.7(-18,-.90)	**0.037**	11	11	3.71(2.68,5.15)
PFNA	Stockholm	40	16	72-14	4.1(2.1,6.2)	**0.001**	16	26	17.2(13.4,22.0)
	Stockholm		8	07-14	-12(-21,13)	0.257	16	25	
	Gothenburg	27	7	07-15	.17(-3.3,3.8)	0.909	7	4	16.4(14.1,19.1)
PFOA	Stockholm	40	16	72-14	.17(-1.4,1.7)	0.824	14	19	46.3(39.9,53.8)
	Stockholm		8	07-14	-8.2(-17,.98)	0.069	9	8.5	
	Gothenburg	27	7	07-15	-6.9(-12,-1.4)	**0.025**	8	6.6	48.4(38.0,61.7)
PFOS	Stockholm	40	16	72-14	-.62(-8.0,-.85)	0.650	21	42	38.5(32.9,45.1)
	Stockholm		8	07-14	-7.4(-13,-1.1)	**0.030**	8	5.7	
	Gothenburg	27	7	07-15	-9.0(-17,.15)	0.052	11	11	43.9(29.8,64.5)
PFTeDA	Stockholm	40	16	72-14	.52(-1.1,2.2)	0.502	14	20	1.12(0.924,1.35)
	Stockholm		8	07-14	5.6(-13,28)	0.508	14	19	
	Gothenburg	27	7	07-15	-.19(-13,14)	0.972	13	17	1.02(0.637,1.63)
PFTriDA	Stockholm	40	16	72-14	3.3(1.8,4.9)	**0.001**	14	18	1.98(1.54,2.53)
	Stockholm		8	07-14	9.3(-9.3,32)	0.275	14	18	
	Gothenburg	27	7	07-15	1.5(-14,20)	0.828	15	21	2.22(1.17,4.18)
PFUDA	Stockholm	40	16	72-14	3.7(2.0,5.4)	**0.001**	15	21	4.61(4.04,5.27)
	Stockholm		8	07-14	-.42(-9.0,39.0	0.910	9	8.1	
	Gothenburg	27	7	07-15	-1.7(-9.5,6.8)	0.621	10	9.7	4.60(3.24,6.52)

13.2.1 Temporal variation

The concentrations of PFDA, PFHxS, PFNA, PFTriDA and PFUDA were increasing significantly over time (3.2-4.1 % per year) whereas a downward trend was observed for FOSA (4.6 % per year, Table 13.1 and Figure 13.3, 13.7, 13.8, 13.12 and 13.13) in human milk from Stockholm. In the human milk samples from Gothenburg significant downward

trends were detected for PFDoDA, PFHxS and PFOA of -8.6, -9.7 and -6.9 % per year, respectively (Table 13.1. and Figure 13.4, 13.7, 13.9). Significant upward-downward Change-Point trends were detected for PFOA (2000), PFHxS (2004) and PFOS (1988), while upward- upward g trends were observed for PFUDA (1984) and PFNA (2010) and downward -upward trends were observed for PFTeDA (1980) (Table 13.2) in human milk from Stockholm. No trend or Change-Point was observed for PFHxA, PFHpA, PFDoDA and PFBS, but for the first three, the majority of the years were below LOQ. PFNA and PFDA showed similar increasing trends in pooled blood serum samples from nursing women living in Uppsala (Glynn et al. 2012). PFHxS concentration was increasing over the entire monitoring period and also during the most recent years in the Uppsala blood samples (Glynn et al. 2012). In contrast, PFHxS showed significant decreasing concentrations from 2004 and onward in the present study. In 2012 parts of Uppsala´s drinking water were found to be contaminated with PFASs, most likely originating from fire-fighting foams used at a military airport just outside Uppsala. PFHxS was one of the substances found in high levels in the drinking water; consequently, ongoing PFHxS contamination could explain the absence of a decrease in concentrations (Gyllenhammar et al. 2015). Decreasing trends (1995-2010) for FOSA, PFOA and PFOS concentrations were reported for the blood samples (Glynn et al. 2012), consistent with our observations in milk and with the phase-out by 3M.

The number of years required to detect an annual change of 10 % for PFASs varied between 8-24 years.

Table 13.2 Change-Point detection for **PFASs** assessed from the annual arithmetic means (pg/ml) in human milk from Stockholm. NY is the total number of years for the various time-series, P(trend) shows the p-value for the log-linear regression, P(CP) shows the p-value for the Change-Point, Year(CP) is the year when the CP occur, b(1), (2) are the slopes of the first and second regression line which also is equal to the average annual percentual change in concentration, P(1), (2) the p-values for the first and second regression line and LOQ/NY show years below level of quantification (LOQ).

PFASs	**P(CP)**	**Year(CP)**	**b(1)**	**P(1)**	**b(2)**	**P(2)**	**LOQ/NY**
FOSA	.072		9.74	.001	-10.67	.002	0/16
PFBS	.116						6/16
PFDA	.147						4/16
PFDoDA	.355						10/16
PFHpA	.557		-1.74	.246	5.99	.661	11/16
PFHxA	.186						9/16
PFHxS	**.001**	2004					0/16
PFNA	**.028**	2010	6.08	.000	3.42	.824	0/16
PFOA	**.000**	2000	4.14	.007	-7.58	.001	0/16
PFTeDA	**.037**	1980	-10.87	.125	2.14	.024	7/16
PFOS	**.000**	1988					0/16
PFTriDA	.437						6/16
PFUDA	**.000**	1984	15.09	.084	.37	.403	2/16

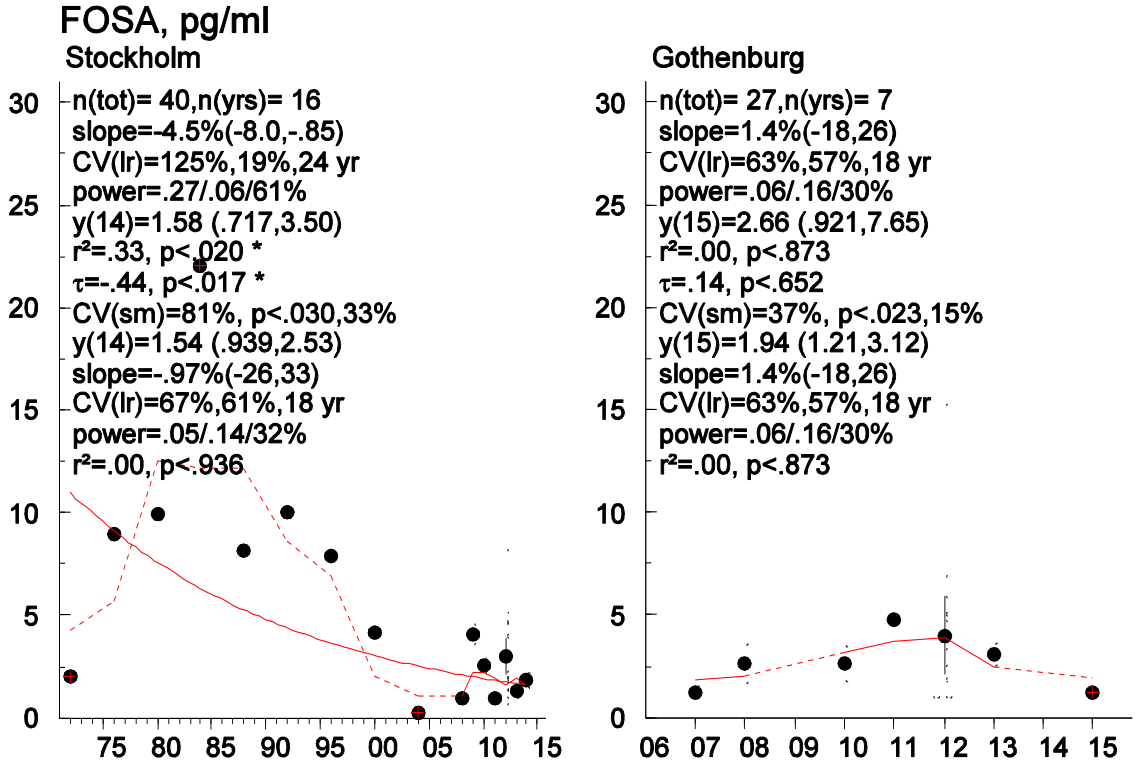

Figure 13.1 Temporal trend of FOSA (pg/ml) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015).

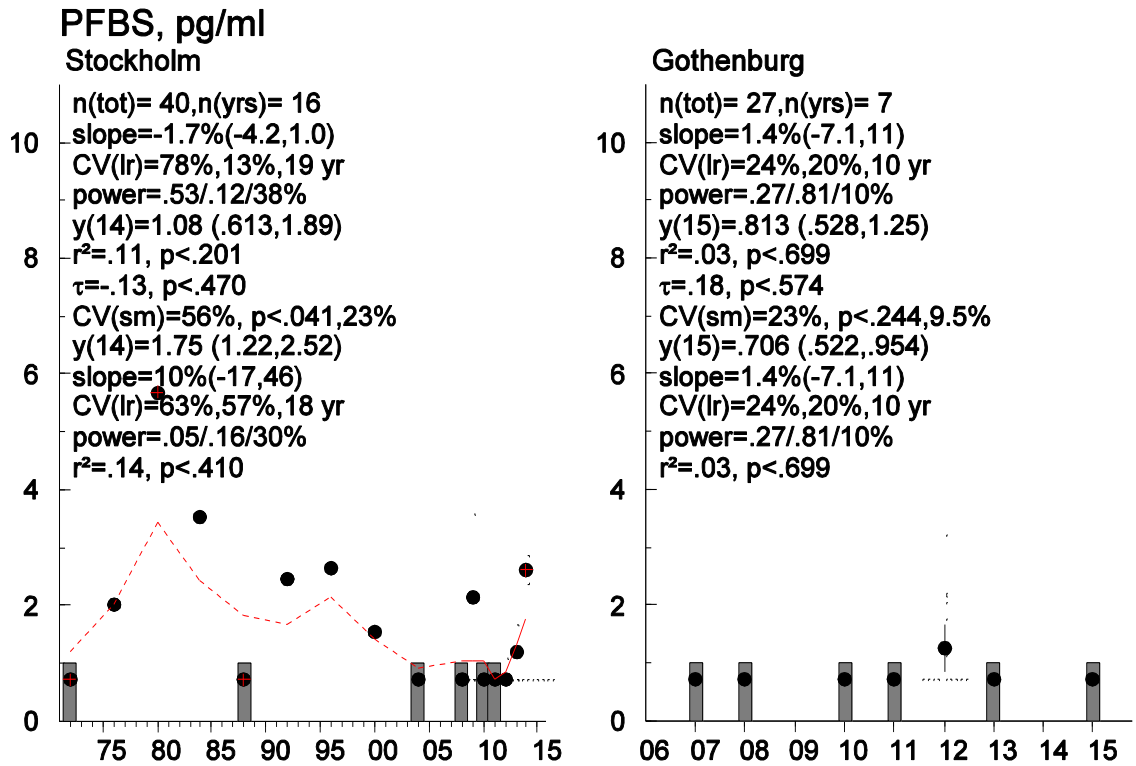

Figure 13.2 Temporal trend of PFBS (pg/ml) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015). The grey bars represent years where all values are below LOQ.

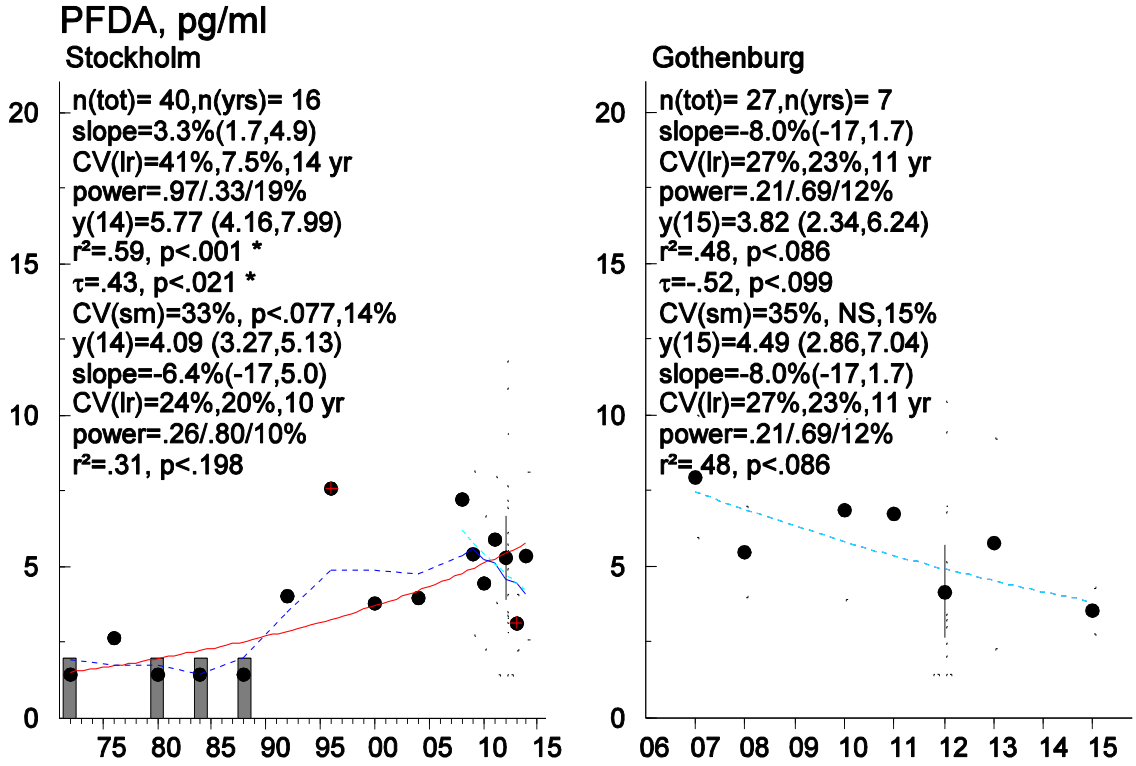

Figure 13.3 Temporal trend of PFDA (pg/ml) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015). The grey bars represent years where all values are below LOQ.

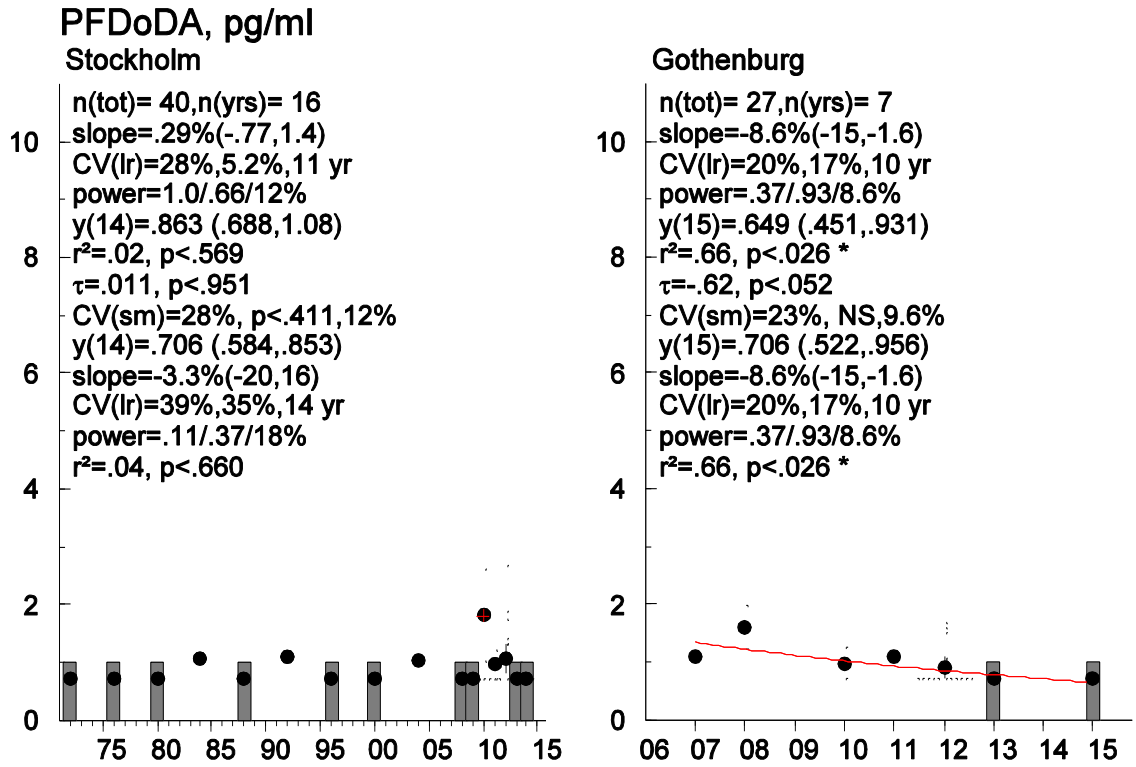

Figure 13.4 Temporal trend of PFDoDA (pg/ml) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015). The grey bars represent years where all values are below LOQ.

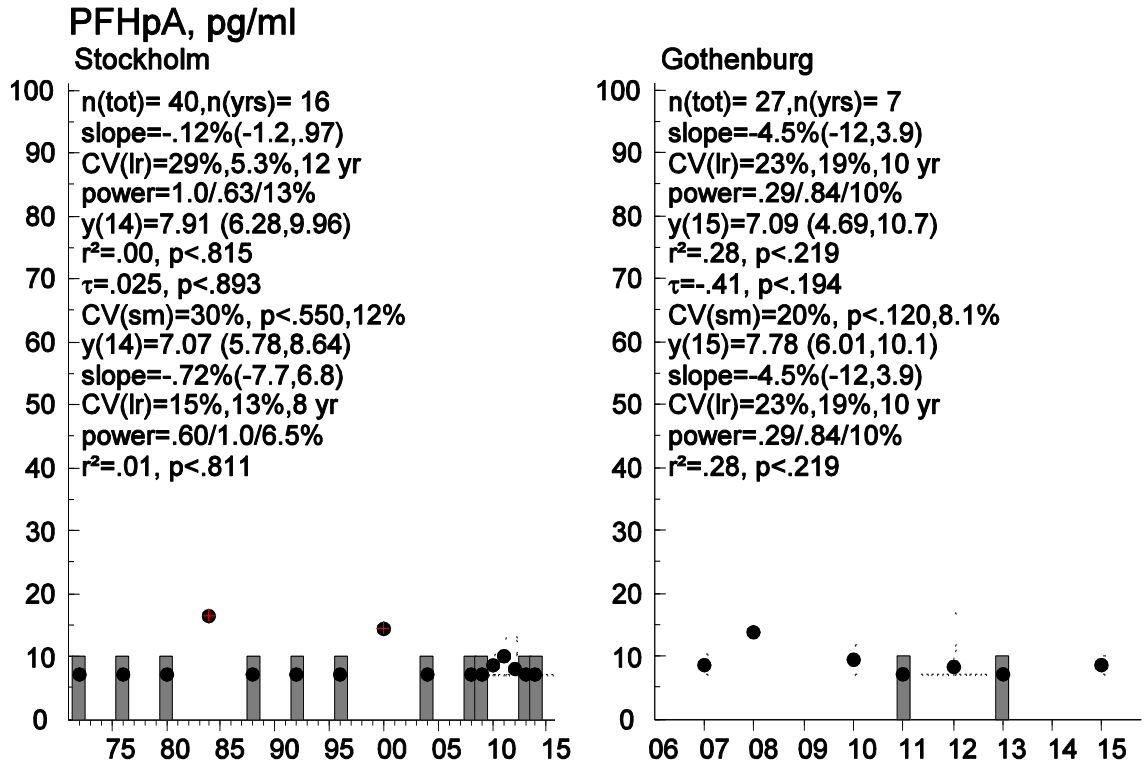

Figure 13.5 Temporal trend of PFHpA (pg/ml) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015). The grey bars represent years where all values are below LOQ.

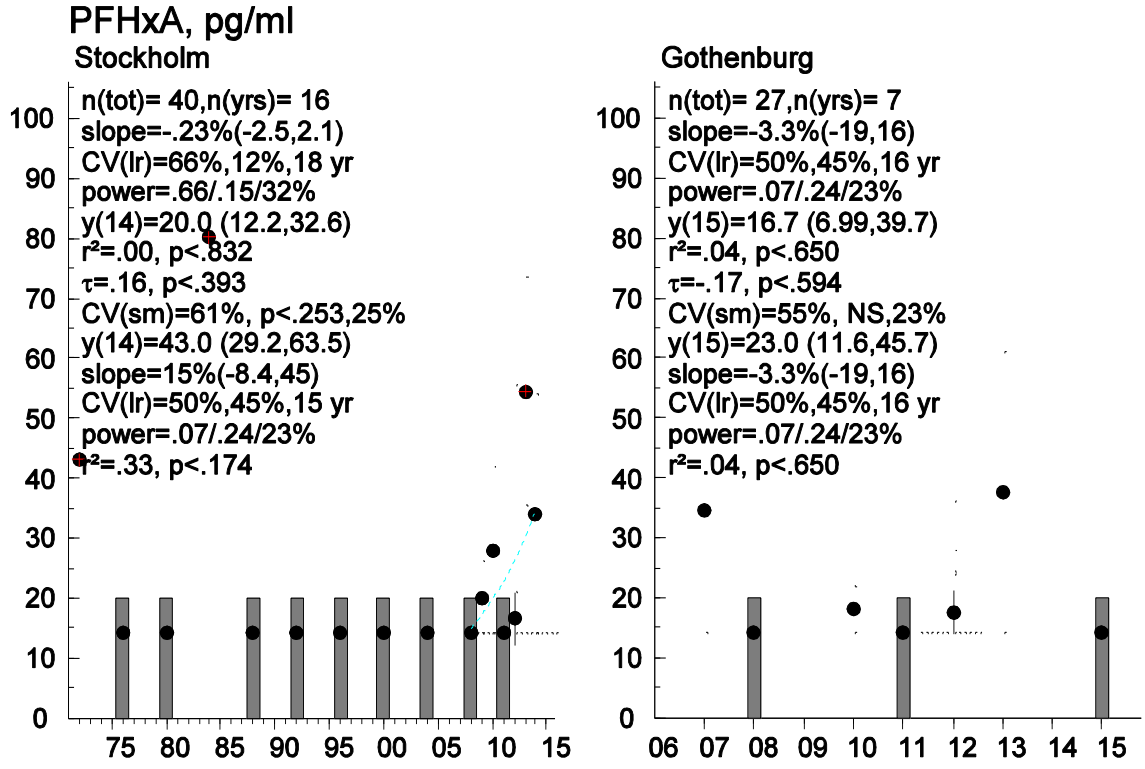

Figure 13.6 Temporal trend of PFHxA (pg/ml) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015). The grey bars represent years where all values are below LOQ.

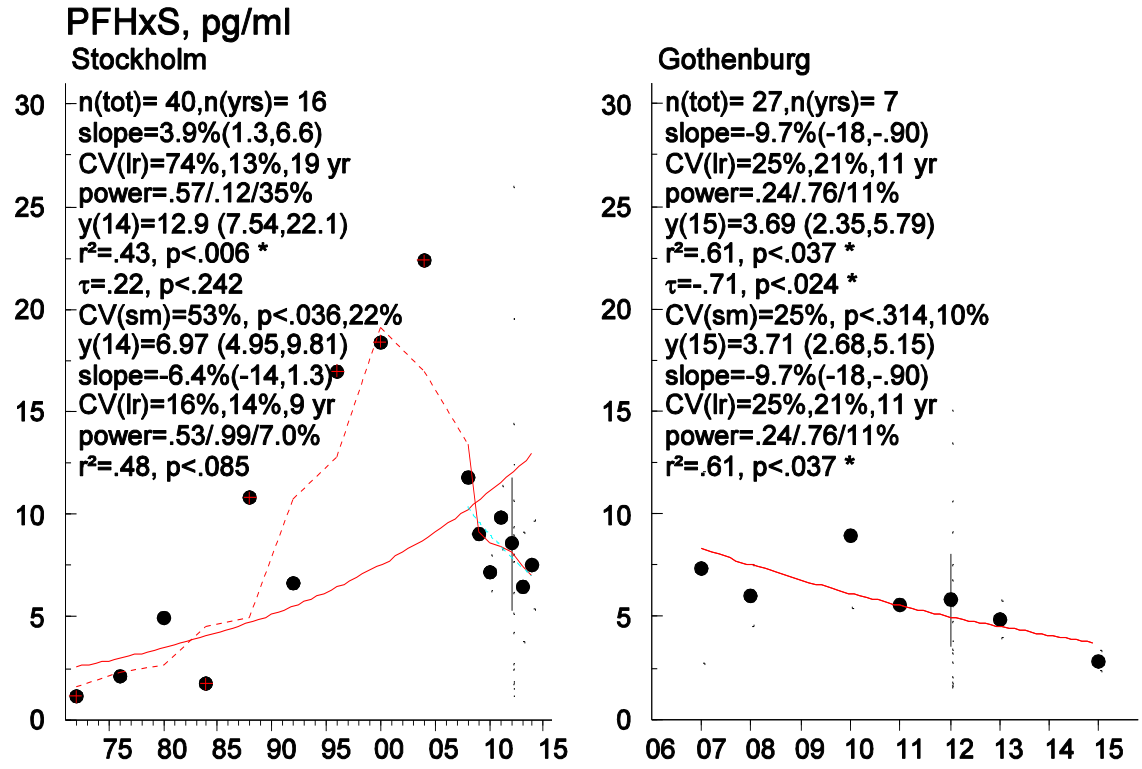

Figure 13.7 Temporal trend of PFHxS (pg/ml) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015).

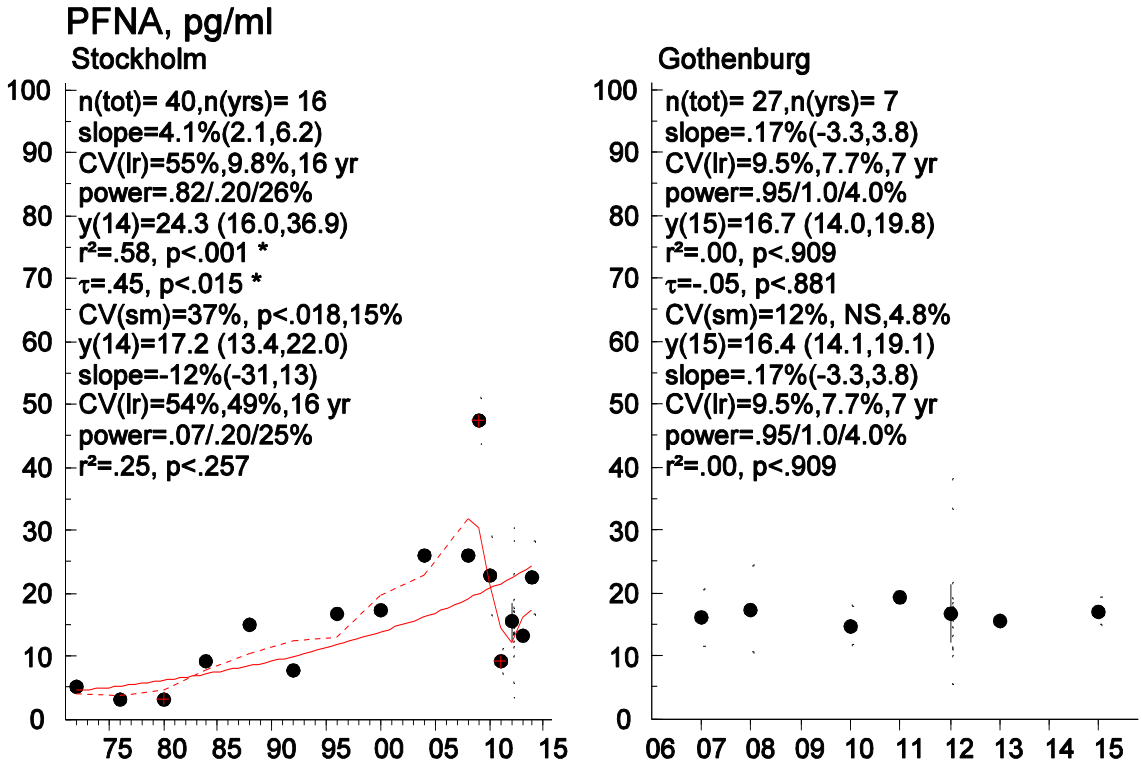

Figure 13.8 Temporal trend of PFNA (pg/ml) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015).

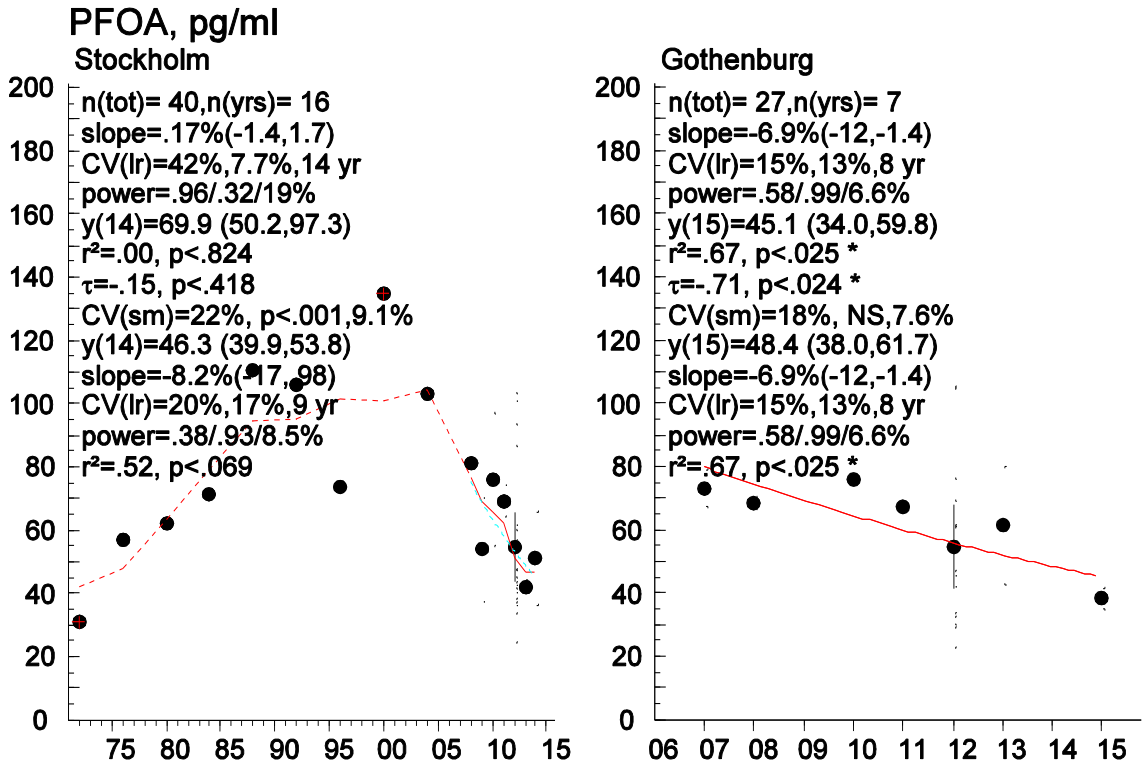

Figure 13.9 Temporal trend of PFOA (pg/ml) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015).

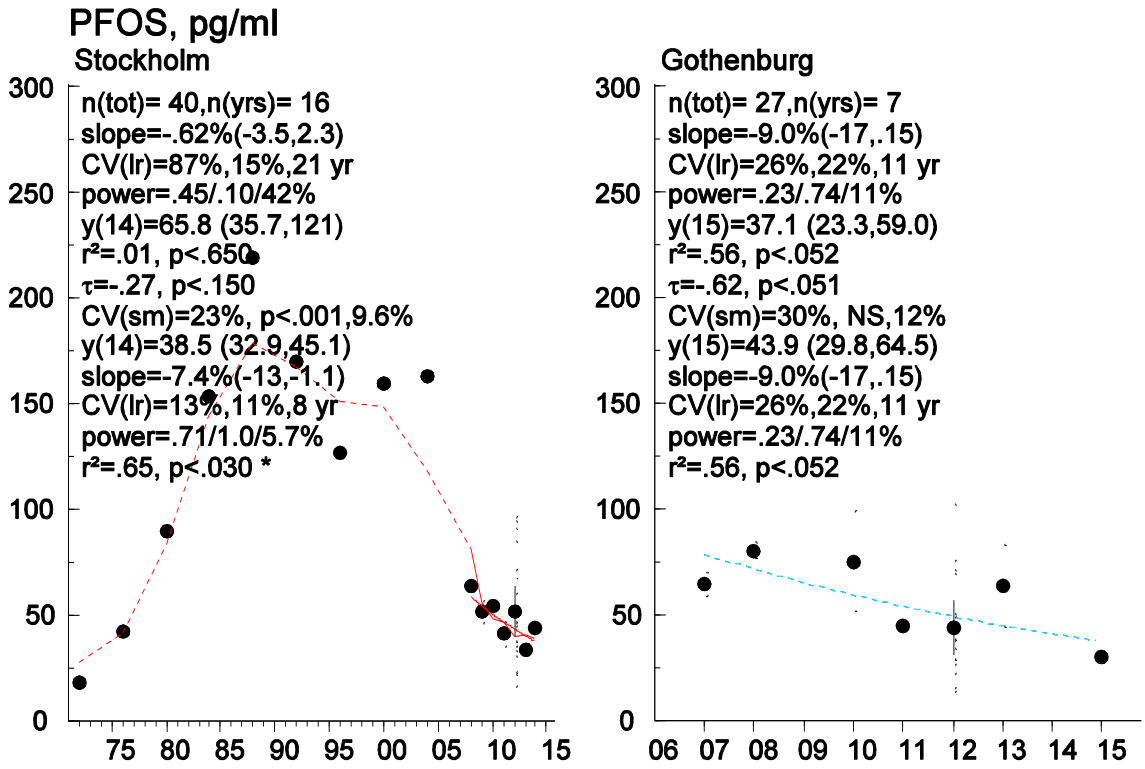

Figure 13.10 Temporal trend of PFOS (pg/ml) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015).

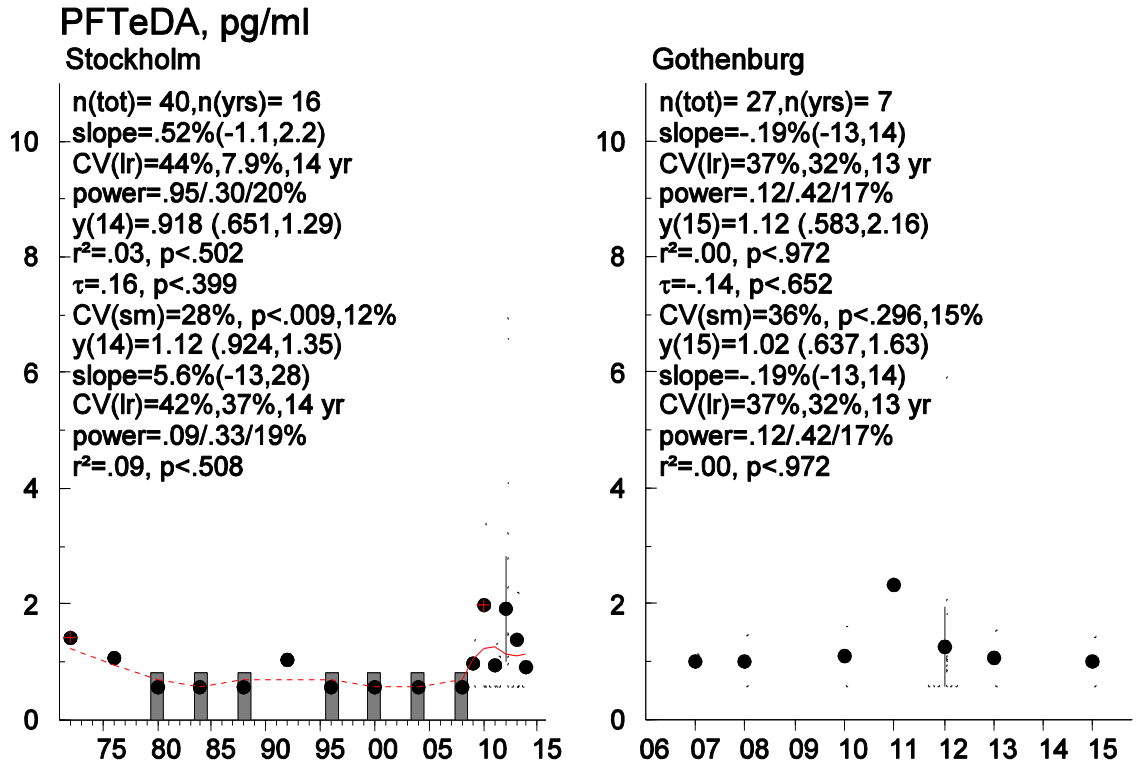

Figure 13.11 Temporal trend of PFTeDA (pg/ml) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015). The grey bars represent years where all values are below LOQ.

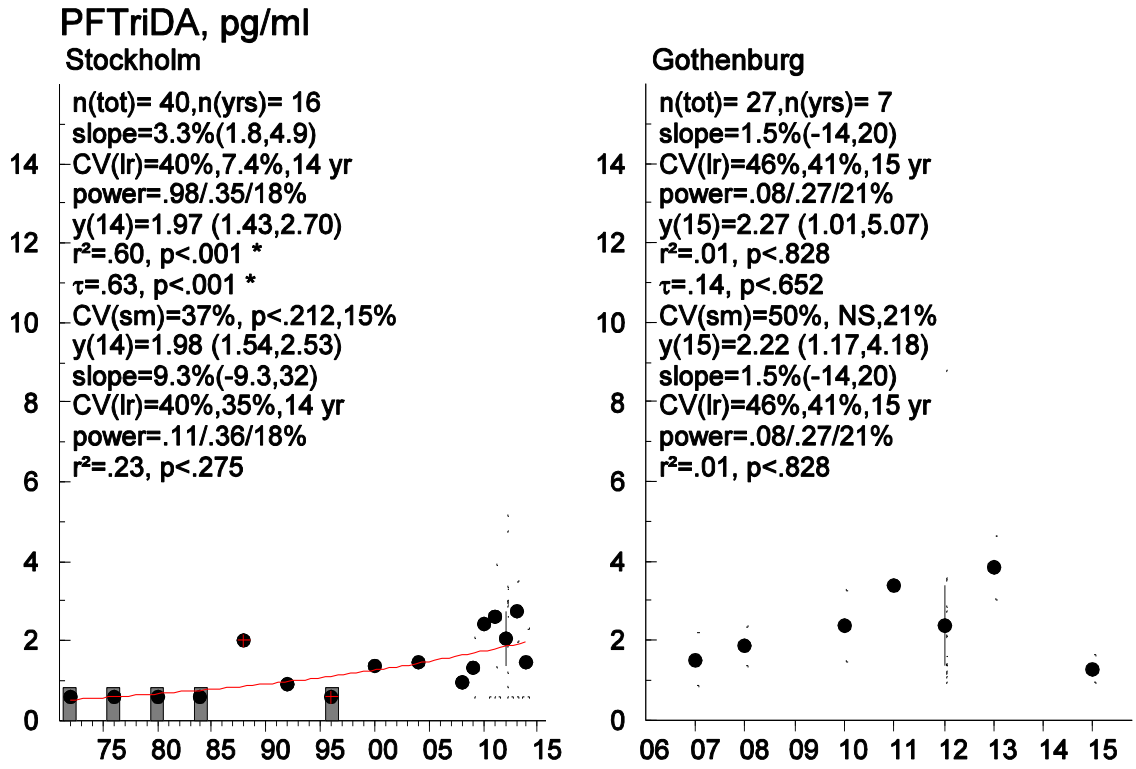

Figure 13.12 Temporal trend of PFTriDA (pg/ml) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015). The grey bars represent years where all values are below LOQ.

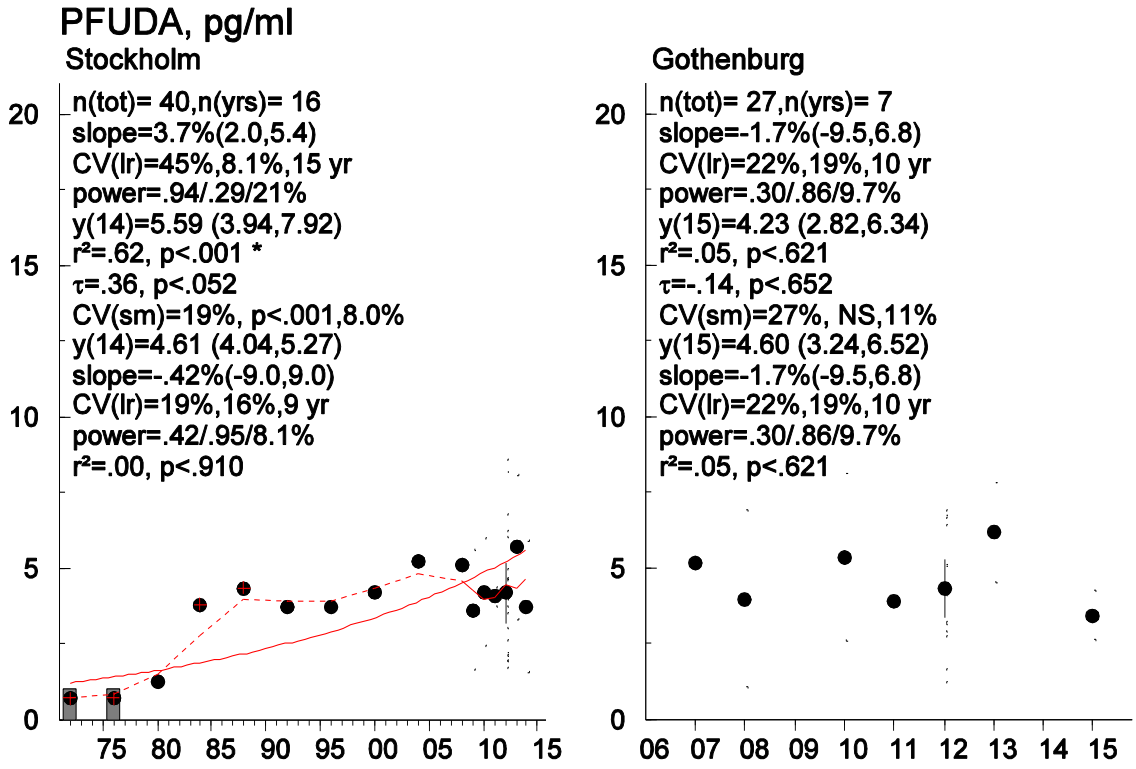

Figure 13.13 Temporal trend of PFUDA (pg/ml) in human milk from Stockholm (1972-2014) and Gothenburg (2007-2015). The grey bars represent years where all values are below LOQ.

13.2.2 Concentrations and spatial differences

The concentration in 2014/2015 (estimated from the smoothed line) was highest for PFOA (46.3 pg/ml Stockholm, 48.4 pg/ml Gothenburg) and PFOS (38.5 pg/ml Stockholm, 43.9 pg/ml Gothenburg) (Table 13.1). PFOS concentrations here were generally lower than concentrations reported in a worldwide review (Fång et al. 2015), which ranged from 40-260 pg/ml (arithmetic mean) for 2006-2010. Another review (Kang et al. 2016), which included studies from 2008-2015 worldwide, reported somewhat lower levels (arithmetic mean) of PFOS in human milk, more in accordance with concentrations in the present study. The PFOA concentration in this study was also in line with concentrations reported previously (Kang et al. 2016) (about 40-150 pg/ml). The levels of PFOS and PFOA in the present study were in the lower range compared to concentrations measured in human milk from Uppsala in 2004. PFOS concentrations had the range 60-470 pg/ml and PFOA 209-492 pg/ml in the Uppsala samples (Kärrman et al. 2007).

The PCA (Figure 13.14) showed no significant difference in PFASs pattern between Stockholm and Gothenburg (2007-2015), which possibly implies that the source and time of contamination was similar between the two cities. A comparison with a known contaminated area, like the Uppsala cohort (Glynn et al. 2012), might result in a significant difference.

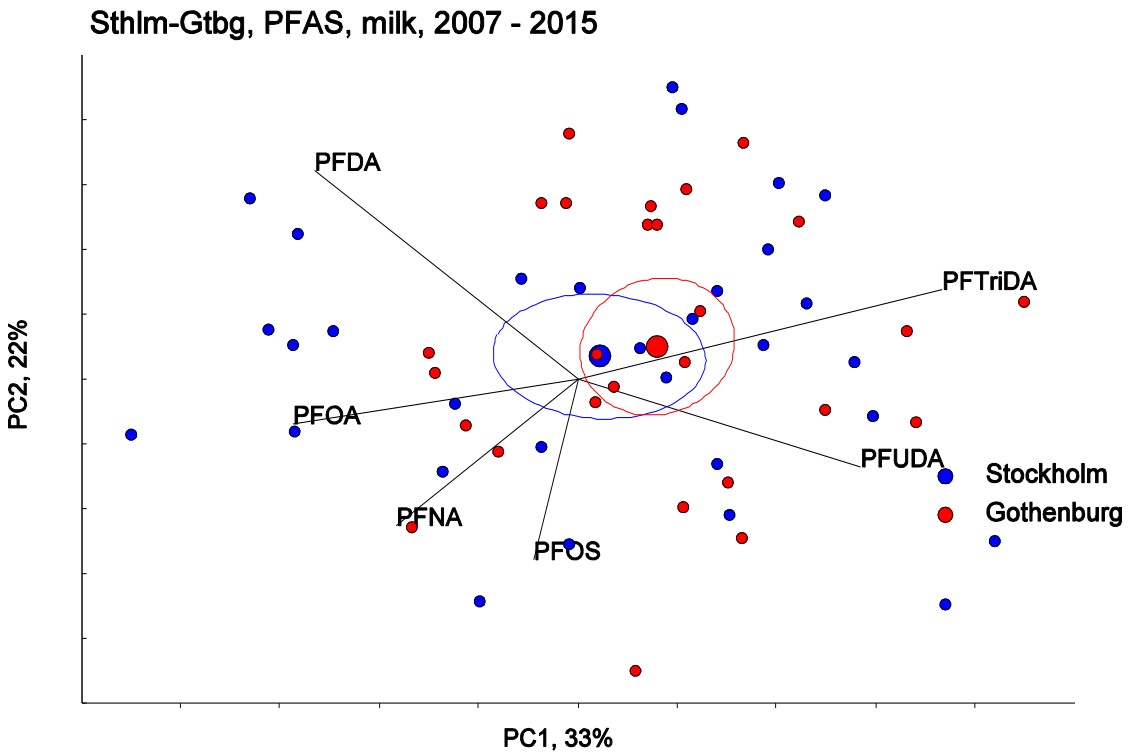

Figure 13.14. PCA (Principal Component Analysis), biplot and Hotellings 95 % confidence ellipses for center of gravity for each group. The figure shows the PFASs (PFOA, PFOS, PFNA, PFDA, PFUDA, PFTriDA) in human milk from Stockholm and Gothenburg (2007-2015).

13.2.3 Individual Variation

The difference in Coefficient of Variation (CV) between mothers sampled the same year (2012) from Stockholm and Gothenburg is illustrated in Figure 13.15. PFTeDA showed the highest CV in human milk from both Gothenburg and Stockholm. PFOA, PFUA and PFNA had the lowest CV. The F-test revealed that there was a significant difference in CV for FOSA (p=.0087) between the two cities, which could indicate a difference in contamination. However, no significant differences in CV were found for the remaining PFASs.

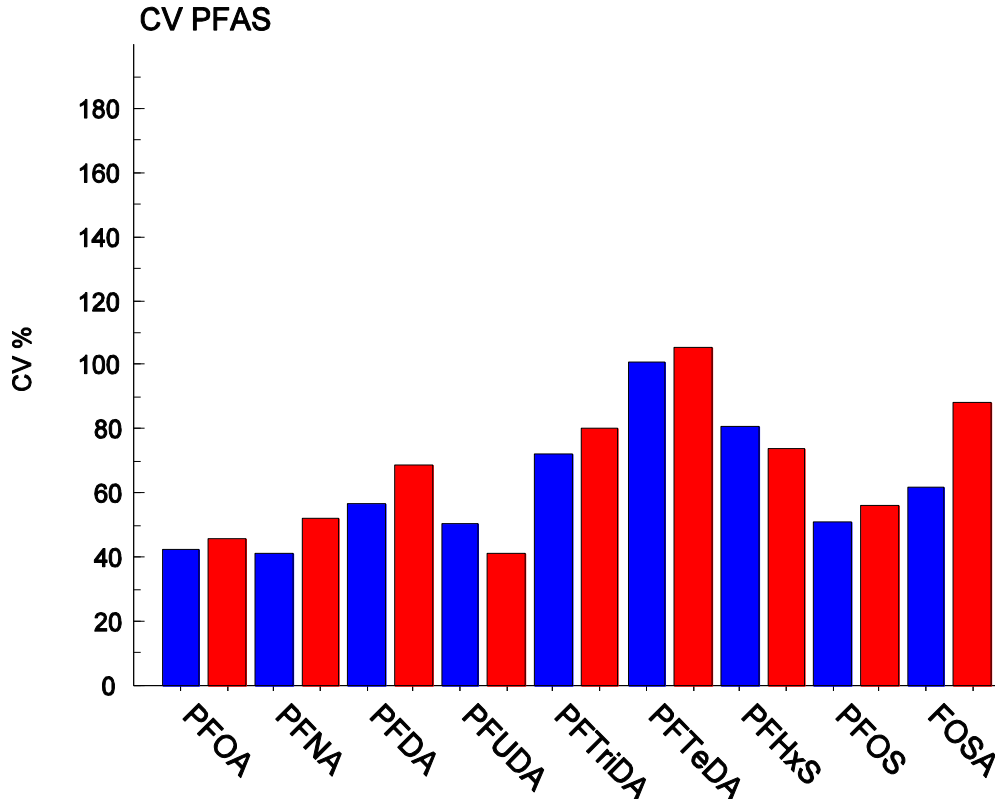

Figure 13.15. CV (Coefficient of Variation) in % in human milk from Stockholm (blue bars) and Gothenburg (red bars).

13.3 Conclusion

The concentrations of PFDA, PFHxS, PFNA, PFTriDA and PFUDA in human milk from Stockholm increased significantly during the whole monitoring period, whereas PFOA concentrations were decreasing. In the human milk samples from Gothenburg significant downward trends were detected for PFDoDA, PFHxS and PFOA and that was also the case for PFOS in Stockholm for the most recent ten year period. The PFOS and PFOA concentrations reported here were comparable to or in the lower end of concentrations reported from other countries. There was no significant difference in the pattern for PFOA, PFOS, PFNA, PFDA, PFUDA and PFTriDA between Stockholm and Gothenburg.

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