The impacts of emission trends of POPs on human concentration dynamics: Lessons learned from a longitudinal study in Norway (1979-2007)

Therese Haugdahl Nøst, [†1,2] Torkjel Manning Sandanger, [†1,2] Evert Nieboer,[3] Jon Øyvind Odland,[2] Knut Breivik[4,5]

[1]NILU - Norwegian Institute for Air Research, the FRAM Centre, P.O. Box 6606 Langnes, NO-9296 Tromsø, Norway;

[2]Department of Community Medicine, Faculty of Health Sciences, UiT - the Arctic University of Norway, P.O. Box 6050 Langnes, NO-9037 Tromsø, Norway;

[3]Department of Biochemistry and Biomedical Sciences, McMaster University, 1280 Main Street West, Hamilton, Ontario, Canada;

[4]NILU - Norwegian Institute for Air Research, P.O. Box 100, NO-2027 Kjeller, Norway;

[5]Department of Chemistry, University of Oslo, P.O. Box 1033, NO-0315 Oslo, Norway.

[†]The authors agree that the first two authors are to be regarded as joint first authors.

Corresponding author: Therese Haugdahl Nøst, Department of Community Medicine, Faculty of Health Sciences, UiT - the Arctic University of Norway, P.O. Box 6050 Langnes, NO-9037 Tromsø, Norway; E-mail: therese.h.nost@uit.no.

Keywords: Blood serum; Persistent organic pollutants; Repeated measurements; Organochlorine pesticides; Polychlorinated biphenyls; Per- and polyfluoroalkyl substances.

Abbreviations: DDE - 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene; DDT - 1,1'-(2,2,2-Trichloroethane-1,1-diyl)bis(4-chlorobenzene); HCB - Hexachlorobenzene; HCHs - Hexachlorocyclohexanes; OCPs - organochlorine pesticides; PCBs - Polychlorinated biphenyls; PFASs - per- and polyfluoroalkyl substances; PFOA - Perfluorooctanoic acid; PFOS - Perfluorooctane sulfonic acid; POPs - Persistent organic pollutants.

Abstract

Background. In this short communication, our focus is on the relationship between human concentrations of select persistent organic pollutants (POPs) and environmental emissions. It is based on a longitudinal study (1979-2007) conducted in Norway.

Objectives. Our aim was to extract general insights from observed and predicted temporal trends in human concentrations of 49 POPs to assist in the design and interpretation of future monitoring studies.

Discussion. Despite considerable decline for polychlorinated biphenyls (PCBs) and organochlorine pesticides (OCPs) since 1986, the sum of the targeted POPs increased from 1979 until 2001, with per- and polyfluorinated alkyl substances (PFASs) dominating recent blood burden measurements. Specifically, the time trends in serum concentrations of POPs, exemplified by PCB-153, 1,1'-(2,2,2-Trichloroethane-1,1-diyl)bis(4-chlorobenzene) (DDT) and perfluorooctane sulfonic acid (PFOS), resembled the trends in available data on their emissions, production or use. These observations suggest that interpretations of human biomonitoring data on persistent compounds must consider historic emissions, which likely vary spatially across the globe. Based on the different temporal trends observed across POP groups, it is evident that generalizations regarding temporal aspects have limitations.

Conclusion. The discussion herein underscores the importance of understanding temporal variations in environmental emissions when designing and interpreting human biomonitoring studies.

Introduction

Humans worldwide are exposed to an array of anthropogenic substances in their everyday lives. The overall increase in the manufacture of man-made chemicals and industrial by-products in the 20th century is deemed responsible (Egeghy et al., 2012). In addition to persistence POPs bioaccumulate, have the potential for long-range transport, and are toxic. Several international legislative agreements place restrictions or bans on the manufacture and use of several POPs. These and other initiatives aim to protect the environment and human health. Regulatory actions have indeed decreased the global manufacture and emissions of POPs (Breivik et al., 2007; Paul et al., 2009; Schenker et al., 2008). Each legacy POP or POP group has a unique emission history that is dictated by its past production and control strategies. For example, the estimated global emissions of PCB-153 in 2016 were ~3% of that in 1970 (Breivik et al., 2016). Since the terminology for estimated 'emissions' in the available literature varies, we define it as including the sum of environmental releases across the chemical life-cycle (manufacturing, use and disposal stages).

Various human biomonitoring studies have demonstrated that blood concentrations of PCBs, OCPs and certain PFASs have decreased in many countries in recent years (Haug et al., 2009; Kato et al., 2011; Schröter-Kermani et al., 2012; Thomsen et al., 2007; Toms et al., 2014; Vo et al., 2008). Clearly, the knowledge of human concentrations and their predictor variables remains fragmented because studies vary in design, targeted study period, geographical location , as well as gender and age of the study subjects (Porta et al., 2008). For example, biomonitoring initiatives have been strongly biased towards industrialised countries as opposed to developing countries. Furthermore, the majority of human biomonitoring studies are of cross-sectional design and do not consider time-dependent changes in emissions when interpreting contaminant concentrations. More complete assessments of contaminant burdens

70 are lacking because most studies represent snapshots that include only a limited fraction of all
71 detectable contaminants.

72 In this commentary, we recapitulate intra-individual changes in concentrations of 24 PCBs, 16
73 OCPs and 9 PFASs measured in a longitudinal study (1979-2007) involving a male
74 Norwegian cohort (Nøst et al., 2013; 2014). Furthermore, we aim to extract features relevant
75 for the design and interpretation of future biomonitoring studies, specifically: (i) temporal
76 trends in relation to current emissions and potential geographical trends; and (ii), the relative
77 and aggregate POP compositions across time.

78

79 Materials and Methods

80 The Tromsø Study is a population-based study in Tromsø (~70,000 inhabitants), which is the
81 largest municipality in Northern Norway. Surveys in 1979, 1986-1987 (hereafter referred to
82 as 1986), 1994-1995 (1994), 2001, and 2007-2008 (2007) allowed for a longitudinal design of
83 repeated measurements. Based on gender, age group and geographic region (Alexander et al.,
84 2006; Bergsten 2004), the study subjects are assumed to have relatively frequent intakes of
85 fish and dietary patterns, characteristic of Northern Norway and be representative for this age
86 group in the region. The concentrations in these men are likely higher compared to the general
87 Norwegian population due to their relatively advanced age and frequent consumption of fish.

88 From 53 men for whom blood samples were available for at least three surveys in the Tromsø
89 study, 254 serum samples were collected. The median ages at the five sampling points were
90 43, 50, 58, 65, and 71. Details of the analytical methodology and quality assurance for the
91 target compounds are provided in Nøst et al. (2013; 2014); all samples were analyzed in 2012
92 at the laboratories of Norwegian Institute for Air Research. The results were compiled for 24
93 PCBs (congeners 18, 28, 33, 47/49, 52, 99, 101, 105, 118, 123, 128, 138, 141, 149, 153, 156,

157, 167, 170, 180, 183, 187, 189, 194), 16 OCPs (*α*-, *β*-, *μ*-HCH, HCB, *trans*-, *cis*-, *oxy*-chlordane, *trans*-, *cis*-nonachlor, Mirex, Toxaphene Parlar 26 and 50, *p,p′*-DDD, *o,p′*-, *p,p′*-DDT, *p,p′*-, *o,p′*-DDE) and 9 PFASs (FOSA, PFDA, PFHpA, PFHpS, PFHxA, PFHxS, PFNA, PFOA, PFOS; for abbreviations see Nøst et al. 2014). Mixed models were used to assess the time trends of POPs in serum, and details of the data treatment and statistical approaches employed were as described in the references mentioned.

Results

The observed longitudinal trends from 1979 to 2007 of PCBs, OCPs, and PFASs in sera of Northern Norwegian males are summarized in Figure 1 and Table 1 (Nøst et al., 2013; 2014). The temporal trends differed among compounds during the 28-year period, and the aggregated POP concentrations increased until 2001. In general, the concentrations of PCBs decreased from 1979 or 1986 on, whereas the OCPs did so from 1979. Summed PFASs increased five-fold from 1979 to 2001 and then decreased; the longer chained perfluoroalkyl carboxylic acids also increased throughout this period.

PFASs, DDTs and PCBs contributed almost equal proportions to the summed concentrations in 1979, while PFASs have dominated subsequently (Table 1 and Figure 1).

The Spearman`s ρ correlations for PCB-153 with other POPs spanning the sampling years were robust ($\rho \geq 0.95$) for many compounds, such as the higher chlorinated PCBs, and moderate ($\rho > 0.6$) for others (e.g., *trans*-Nonachlor, *p,p*'-DDE, toxaphene Parlar 26 and HCB). Correlations were weaker for HCHs ($\rho<0.6$) and most PFASs (e.g. $\rho<0.3$ for PFOA and $\rho<0.4$ for PFOS).

Discussion

Interpretation of temporal trends of POPs in Northern Norway in relation to emissions inventories

Figure 1 reveals that the summed concentrations of the measured POPs increased considerably from 1979 to 2001 and was driven primarily by the increase in PFASs, decreasing thereafter (2001-2007). Compound-specific changes in human concentrations during this observation period appear convincingly coherent with those depicted for past emissions for individual or groups of contaminants. This is illustrated in Figure 2 for the divergent time trends shown for PCBs, OCPs and PFASs. As there has been no production of any of these compounds in Norway, exposure is likely linked to a combination of historic imports and uses, long-range transport (Armitage et al., 2009; Mantseva et al., 2004), and their presence in food items (Haug et al., 2010). Our biomonitoring and modelling results highlight that human temporal trends are also influenced by compound-specific delays between chemical imports, environmental emissions, and degradation/elimination rates (Alcock et al., 2000; Quinn and Wania 2012; Ritter et al., 2009). Using PCB-153 as an example (see Figure 3), we conclude that these delays may be significant and reflect: (i) time-lags between production/import and emissions due to the long lifetime of PCB-containing products; and (ii), delays between peaks in emissions, environmental/food-chain exposures and human concentrations. Further, the timing of peaks in environmental exposures for each compound is modulated by media-specific degradation rates as well as the modes of environmental transport. Estimations of these processes by mechanistic modeling are presented for PCB-153 in Figure 3 and are discussed by Breivik et al. (2010) and Quinn and Wania (2012).

Clearly, accurate knowledge of emissions for various compounds over time is critical for the interpretation of time trends. Dynamic multimedia mechanistic models may provide

quantitative links between emissions and human exposures (MacLeod et al., 2010). For certain PCBs, estimates of the median concentrations in the present study group were obtained from one such model, the CoZMoMAN model, which convincingly reconstructed the measured concentrations and their time trends (Nøst et al., 2013). This strengthened our hypothesis that empirical time trends are largely dictated by changes in emissions. While significant efforts have been invested in the development of emission inventories for some POPs that are emitted as by-products of combustion (e.g., Pacyna and Graedel, 1995), obtaining accurate information on rates of production, use and/or emissions of intentionally produced organic contaminants has proven challenging. Confidentiality issues appear to be partly responsible (Breivik et al., 2012). Further, fate properties are divergent for different POPs in various environmental media and humans, including degradation and metabolism/elimination half-lives, respectively (Figure 3). This also highlights a chemical-specific approach to POPs, even within groups of related compounds. From the clear links between trends in emissions and human concentrations of POPs observed in the Tromsø study, it seems pertinent to assess whether similar or divergent temporal trends in human body burdens might be anticipated globally.

Reduced emissions of PCBs and OCPs has had an impact on human blood concentrations, but these compounds constitute only a small fraction of the total exposure to contaminants in the Norwegian cohort by 2007 (Nøst et al., 2013; 2014). Similar declines across recent decades are reported in many industrialized countries (e.g., Hagmar et al., 2006; Thomsen et al., 2007; Vo et al., 2008). Phasing out and placing restrictions on use of PFOS and PFOA have led to decreasing concentrations after 2001, but their contributions to total body burden nevertheless remain high in 2007. The declines of PFOS and PFOA in recent years are also described for other industrialized countries (Gebbink et al., 2015; Haug et al., 2009; Kato et al., 2011; Schröter-Kermani et al., 2012). As observed for PCBs, OCPs and PFASs, the lowering of emissions has clearly been effective in reducing human concentrations in Tromsø, and this

pattern is likely to occur in many other industrialized countries where these chemicals were extensively produced and/or used.

One factor that may cause divergent trends globally is attributed to the long lifetime of various use categories of products containing organic contaminants; they represent potential emission sources long after initial regulatory actions (Diamond et al., 2015). An example is the elevated emissions from informal waste or recycling processes in developing regions, such as of PCBs and other organic contaminants (e.g., PBDEs) released from waste electrical and electronic equipment (Breivik et al., 2011; Robinson 2009; Zhang et al., 2012). Thus the effectiveness of reducing human exposure to POPs in many countries can be improved by adopting environmentally sound practices to remove and process products and materials containing these compounds. Furthermore, export of e-wastes to developing regions offer a disturbing example of how temporal emissions trends of POPs may be spatially and temporally separated from those in areas where these chemicals were produced and used (Breivik et al., 2011). Indeed, elevated concentrations in humans in areas influenced by such activities have been reported (Grant et al., 2013; Wang et al., 2014; Wittsiepe et al., 2015). In Ghana, known to import of electronic waste (Schluep et al., 2011), concentrations of PCBs and PBDEs in breast milk samples increased from 2004 to 2009 (Asante et al., 2011). Furthermore, recent plasma concentrations of PCBs in Ghanaian immigrants to the Canary Islands (Luzardo et al., 2014) were higher compared to those in the Norwegian cohort even in 1979 (respectively, medians of 503 and 360 ng/g lipid weight for PCB-153). Although temporal trends of the legacy POPs clearly indicate reduced human exposure to these compounds in industrialized countries, the trends in developing countries do not necessarily conform. This illustrates that emission trends and human exposures may be spatially variable across the globe, due to transboundary exports of hazardous waste for example. Other factors may also create differences in temporal trends even in a post-ban situation, with population

dietary transitions an example (Quinn et al., 2012). Consequently, results from regional biomonitoring studies are not necessarily universally applicable. Temporal trends in emissions and influences of population-specific confounding factors must be considered.

Dynamic POP compositions

The 49 compounds included in this longitudinal study enabled a detailed assessment of how the sum of all compounds and their relative contributions have varied across the 30-year study period. Compound-specific and time-variant emissions of POPs have resulted in complex and dynamic burdens of POPs in human blood as depicted in Figure 1. Although age and birth year are confounded in cross-sectional studies, the time trends in this longitudinal study were confounded only by age. Clearly, the interpretation of differences in POP concentrations due to age (both within and between persons) in biomonitoring studies are conditional on the time of sampling and the age distribution of a study population in relation to historic emissions (Alcock et al., 2000; Quinn and Wania, 2012).

The changes in relative proportions of POPs are also reflected in the inter-compound correlations. Overall, moderate or strong correlations over time suggest similar emission histories, exposure pathways and persistence in the environment and humans. PCB-153 has been suggested as a suitable marker for PCBs and other POPs (Covaci et al., 2002; Glynn et al., 2000). As reported above, inter-correlations between PCB-153 and other PCBs (e.g., PCB-180) were very robust in the Norwegian study, and this was also evident for OCPs like HCB. By contrast, the newer POPs like PFOA and PFOS did not associate with PCB-153 at any time point. Thus, the latter is less representative of the total exposure to halogenated compounds in the Norwegian cohort in 2007 compared to 1979, and thereby its potential as a single marker has been reduced in the years beyond the peak exposure to legacy POPs.

Subsequently, the potential use of PCB-153 as a marker for summed POP exposure that include emerging contaminants with dissimilar physicochemical properties and historic emissions has been diminished.

The number of organic and inorganic chemicals introduced on the global market has increased substantially in the past few decades, and more than 100,000 substances are used commercially today (Egeghy et al., 2012). It is thus likely that the human body burden of contaminants include chemicals currently in use that have not received the attention of researchers, and thus could indeed be contaminants of concern (i.e., based on persistence, bioaccumulation potential, and toxicity; Arnot et al., 2012).

Based on the above considerations, it appears fair to hypothesize that the summed concentrations of POPs described in Figure 1 cover merely a fraction of the chemicals present in humans today. Indeed, a number of other contaminants have been detected in human blood in Norwegian studies, including pentachlorophenol and hydroxylated PCBs (Rylander et al., 2012) and emerging brominated flame retardants (Thomsen et al., 2002). Furthermore, the screening of contaminants in the US NHANES monitoring studies has targeted 267 chemicals, and many of them were detected in serum/blood (CDC 2015; Crinnion 2010). Non-POP compounds with short half-lives have recently been quantified in humans such as parabens in Norwegians (Sandanger et al., 2011), although continuous use appears to lead to elevated exposures. Overall, both summed concentrations as well as the complexity of the total human burden of contaminants can be expected to increase in the coming years. Thus ongoing monitoring of human contaminant concentrations should ideally include both legacy pollutants as well as chemicals still produced and used.

Concluding remarks

As exemplified by PCB-153, DDT and PFOS, the time trends in human concentrations of POPs in this longitudinal sample dataset resemble those of their production, use and emission. Our findings highlight the importance of available and accurate data on trends of emissions of individual substances to interpret human biomonitoring studies. A complicating factor is that the trends described may vary spatially across the globe. To address this dimension, informal e-waste recycling and increasing concentrations reported in certain countries where this occurs serves as an example that could guide the selection of geographical areas relevant for conducting related human biomonitoring studies. Clearly, the blood compartment burden of POPs is dynamic, and thus is likely to increase in complexity related to ongoing exposures to compounds currently in use. Future biomonitoring efforts are encouraged to target a broad range of compounds with different physicochemical properties and populations experiencing unique and divergent emission histories.

Acknowledgements: The authors declare they have no competing financial interests. The project was financially supported by the Northern Norway Regional Health Authority, the Fram Centre and the Norwegian Research Council (FRIPRO #213577). The authors are grateful to all study participants.

References

Alcock, R.E., Sweetman, A.J., Juan, C.Y., Jones, K.C. 2000. A generic model of human lifetime exposure to persistent organic contaminants: Development and application to PCB-101. Environ. Pollut. 110, 253-265.

Alexander, J., Frøyland, L., Hemre, G., Jacobsen, B.K., Lund, E., Meltzer, H. 2006. Et helhetssyn på fisk og annen sjømat i norsk kosthold [in Norwegian] Oslo, Norway. Norwegian Scientific Committee for Food Safety. Available from: www.vkm.no/dav/a2805d6a8c.pdf

Armitage, J.M., Schenker, U., Scheringer, M., Martin, J.W., MacLeod, M., Cousins, I.T. 2009. Modeling the global fate and transport of perfluorooctane sulfonate (PFOS) and precursor compounds in relation to temporal trends in wildlife exposure. Environ. Sci. Technol. 43, 9274-9280.

Arnot, J.A., Brown, T.N., Wania, F., Breivik, K., McLachlan, M.S. 2012. Prioritizing chemicals and data requirements for screening-level exposure and risk assessment. Environ. Health Perspect. 120, 1565-1570.

Asante, K.A., Adu-Kumi, S., Nakahiro, K., Takahashi, S., Isobe, T., Sudaryanto, A. et al. 2011. Human exposure to PCBs, PBDEs and HBCDs in Ghana: Temporal variation, sources of exposure and estimation of daily intakes by infants. Environ. Int. 37, 921-928.

Bergsten, C. 2004. Fish and game study, part B. (The consumption of foods that may be important when assessing the dietary intake of mercury, cadmium and PCB/dioxins, with a focus on population groups living on the coast and in the inland of Norway) [in Norwegian] Oslo, Norway. Norwegian Food Safety Authority. Available from: www.mattilsynet.no/mattilsynet/multimedia/archive/00016/Fisk_og_vilt__Fish_a_16664a.pdf

Breivik, K., Sweetman, A., Pacyna, J.M., Jones, K.C. 2007. Towards a global historical emission inventory for selected PCB congeners—a mass balance approach: 3. An update. Sci. Tot. Environ. 377, 296-307.

Breivik, K., Czub, G., McLachlan, M.S., Wania, F. 2010. Towards an understanding of the link between environmental emissions and human body burdens of PCBs using CoZMoMAN. Environ. Int. 36, 85-91.

Breivik, K., Gioia, R., Chakraborty, P., Zhang, G., Jones, K.C. 2011. Are reductions in industrial organic contaminants emissions in rich countries achieved partly by export of toxic wastes? Environ. Sci. Technol. 45, 9154-9160.

Breivik, K., Arnot, J.A., Brown, T.N., McLachlan, M.S., Wania, F. 2012. Screening organic chemicals in commerce for emissions in the context of environmental and human exposure. J. Environ. Monitor. 14, 2028-2037.

Breivik, K., Armitage, J.M., Wania, F., Sweetman, A.J., Jones, K.C. 2016. Tracking the global distribution of persistent organic pollutants accounting for e-waste exports to developing regions. Env. Sci. Technol. 50, 798-805.

CDC (Centers for Disease Control and Prevention). 2015. Fourth National Report on Human Exposure to Environmental Chemicals, Updated Tables, February 2015. Atlanta, GA: Centers for Disease Control and Prevention. Available: http://www.cdc.gov/biomonitoring/pdf/FourthReport_UpdatedTables_Feb2015.pdf [accessed 10 October 2015].

Covaci, A., Koppen, G., Van Cleuvenbergen, R., Schepens, P., Winneke, G., van Larebeke, N. et al. 2002. Persistent organochlorine pollutants in human serum of 50–65 years old women in the Flanders environmental and health study (FLEHS). Part 2: Correlations among PCBs, PCDD/PCDFs and the use of predictive markers. Chemosphere 48, 827-832.

Crinnion, W.J. 2010. The CDC fourth national report on human exposure to environmental chemicals: What it tells us about our toxic burden and how it assists environmental medicine physicians. Altern. Med. Rev. 15, 101-109.

Diamond, M.L., de Wit, C.A., Molander, S., Scheringer, M., Backhaus, T., Lohmann, R. et al. 2015. Exploring the planetary boundary for chemical pollution. Environ. Int. 78, 8-15.

Egeghy, P.P., Judson, R., Gangwal, S., Mosher, S., Smith, D., Vail, J. et al. 2012. The exposure data landscape for manufactured chemicals. Sci. Tot. Environ. 414, 159-166.

309 Gebbink, W.A., Glynn, A., Berger, U. 2015. Temporal changes (1997–2012) of perfluoroalkyl acids
310 and selected precursors (including isomers) in Swedish human serum. Environ. Pollut. 199, 166-173.
311 Glynn, A., Wolk, A., Aune, M., Atuma, S., Zettermark, S., Mæhle-Schmid, M. et al. 2000. Serum
312 concentrations of organochlorines in men: A search for markers of exposure. Sci. Tot. Environ. 263,
313 197-208.
314 Grant, K., Goldizen, F.C., Sly, P.D., Brune, M.-N., Neira, M., van den Berg, M. et al. 2013. Health
315 consequences of exposure to e-waste: A systematic review. Lancet Glob. Health 1, e350-e361.
316 Haug, L.S., Thomsen, C., Becher, G. 2009. Time trends and the influence of age and gender on serum
317 concentrations of perfluorinated compounds in archived human samples. Environ. Sci. Technol. 43,
318 2131-2136.
319 Haug, L.S., Salihovic, S., Jogsten, I.E., Thomsen, C., van Bavel, B., Lindström, G. et al. 2010. Levels
320 in food and beverages and daily intake of perfluorinated compounds in Norway. Chemosphere 80,
321 1137-1143.
322 Kato, K., Wong, L.-Y., Jia, L.T., Kuklenyik, Z., Calafat, A.M. 2011. Trends in exposure to
323 polyfluoroalkyl chemicals in the U.S. population: 1999−2008. Environ. Sci. Technol. 45, 8037-8045.
324 Luzardo, O.P., Boada, L.D., Carranza, C., Ruiz-Suárez, N., Henríquez-Hernández, L.A., Valerón, P.F.,
325 et al., 2014. Socioeconomic development as a determinant of the levels of organochlorine pesticides
326 and PCBs in the inhabitants of Western and Central African countries. Sci. Tot. Environ. 497, 97-105.
327 MacLeod, M., Scheringer, M., McKone, T.E., Hungerbuhler, K. 2010. The state of multimedia mass-
328 balance modeling in environmental science and decision-making. Environ. Sci. Technol. 44, 8360-
329 8364.
330 Mantseva, E., Dutchak, S., Rozovskaya, O., Shatalov, V. 2004. EMEP contribution to the preparatory
331 work for the review of the CLRTAP protocol on persistent organic pollutants. EMEP MSC-E
332 Information Note 5.
333 Nøst, T.H., Breivik, K., Fuskevåg, O.-M., Nieboer, E., Odland, J.Ø., Sandanger, T.M. 2013. Persistent
334 organic pollutants in Norwegian men from 1979 to 2007: Intraindividual changes, age–period–cohort
335 effects, and model predictions. Environ. Health Persp. 121, 1292-1298.
336 Nøst, T.H., Vestergren, R., Berg, V., Nieboer, E., Odland, J.Ø., Sandanger, T.M. 2014. Repeated
337 measurements of per- and polyfluoroalkyl substances (PFASs) from 1979 to 2007 in males from
338 Northern Norway: Assessing time trends, compound correlations and relations to age/birth cohort.
339 Environ. Int. 67, 43-53.
340 Pacyna, J., Graedel, T. 1995. Atmospheric emissions inventories: Status and prospects. Annu. Rev.
341 Energ. Env. 20, 265-300.
342 Paul, A.G., Jones, K.C., Sweetman, A.J. 2009. A first global production, emission, and environmental
343 inventory for perfluorooctane sulfonate. Environ. Sci. Technol. 43, 386-392.
344 Porta, M., Puigdomčnech, E., Ballester, F., Selva, J., Ribas-Fitó, N., Llop, S. et al. 2008. Monitoring
345 concentrations of persistent organic pollutants in the general population: The international experience.
346 Environ. Int. 34, 546-561.
347 Quinn, C.L., Armitage, J.M., Breivik, K., Wania, F. 2012. A methodology for evaluating the influence
348 of diets and intergenerational dietary transitions on historic and future human exposure to persistent
349 organic pollutants in the Arctic. Environ. Int. 49, 83-91.
350 Quinn, C.L., Wania, F. 2012. Understanding differences in the body burden-age relationships of
351 bioaccumulating contaminants based on population cross-sections versus individuals. Environ. Health
352 Persp. 120, 554-559.
353 Ritter, R., Scheringer, M., MacLeod, M., Schenker, U., Hungerbühler, K. 2009. A multi-individual
354 pharmacokinetic model framework for interpreting time trends of persistent chemicals in human
355 populations: Application to a postban situation. Environ. Health Persp. 117, 1280-1286.
356 Robinson, B.H. 2009. E-waste: An assessment of global production and environmental impacts. Sci.
357 Tot. Environ. 408, 183-191.
358 Rylander, C., Lund, E., Frøyland, L., Sandanger, T.M. 2012. Predictors of PCP, OH-PCBs, PCBs and
359 chlorinated pesticides in a general female Norwegian population. Environ. Int. 43, 13-20.
360 Sandanger, T.M., Huber, S., Moe, M.K., Braathen, T., Leknes, H., Lund, E. 2011. Plasma
361 concentrations of parabens in postmenopausal women and self-reported use of personal care products:
362 The NOWAC postgenome study. J. Expo. Sci. Environ. Epidemiol. 21, 595–600.

Schenker, U., Scheringer, M., Hungerbühler, K. 2008. Investigating the global fate of DDT: Model evaluation and estimation of future trends. Environ. Sci. Technol. 42, 1178-1184.
Schluep, M., Manhart, A., Osibanjo, O., Rochat, D., Isarin, N., Mueller, E. Where are WEEE in Africa. Findings from the Basel convention e-waste Africa programme. Secretariat of the Basel Convention: Châtelaine, Switzerland. Available: http://www.basel.int/Implementation/TechnicalAssistance/EWaste/EwasteAfricaProject/Publications/tabid/2553/Default.aspx [accessed 12 September 2015].
Schröter-Kermani, C., Müller, J., Jürling, H., Conrad, A., Schulte, C. 2012. Retrospective monitoring of perfluorocarboxylates and perfluorosulfonates in human plasma archived by the German Environmental Specimen Bank. Int. J. Hyg. Environ. Health 216, 633–640.
Thomsen, C., Lundanes, E., Becher, G. 2002. Brominated flame retardants in archived serum samples from Norway: A study on temporal trends and the role of age. Environ. Sci. Technol. 36, 1414-1418.
Thomsen, C., Liane, V.H., Becher, G. 2007. Automated solid-phase extraction for the determination of polybrominated diphenyl ethers and polychlorinated biphenyls in serum-application on archived Norwegian samples from 1977 to 2003. J. Chromatogr. B 846, 252-263.
Toms, L.M.L., Thompson, J., Rotander, A., Hobson, P., Calafat, A.M., Kato, K. et al. 2014. Decline in perfluorooctane sulfonate and perfluorooctanoate serum concentrations in an Australian population from 2002 to 2011. Environ. Int. 71, 74-80.
Vo, T.T., Gladen, B.C., Cooper, G.S., Baird, D.D., Daniels, J.L., Gammon, M.D. et al. 2008. Dichlorodiphenyldichloroethane and polychlorinated biphenyls: Intraindividual changes, correlations, and predictors in healthy women from the Southeastern United States. Cancer Epidemiol. Biomarkers Prev 17, 2729-2736.
Wang, Y., Xu, M., Jin, J., He, S., Li, M., Sun, Y. 2014. Concentrations and relationships between classes of persistent halogenated organic compounds in pooled human serum samples and air from Laizhou bay, China. Sci. Tot. Environ. 482–483, 276-282.
Wittsiepe, J., Fobil, J.N., Till, H., Burchard, G.-D., Wilhelm, M., Feldt, T. 2015. Levels of polychlorinated dibenzo-p-dioxins, dibenzofurans (PCDD/Fs) and biphenyls (PCBs) in blood of informal e-waste recycling workers from Agbogbloshie, Ghana, and controls. Environ. Int. 79, 65-73.
Zhang, T., Huang, Y.-R., Chen, S.-J., Liu, A.-M., Xu, P.-J., Li, N. et al. 2012. PCDD/Fs, PBDD/Fs, and PBDEs in the air of an e-waste recycling area (Taizhou) in China: Current levels, composition profiles, and potential cancer risks. J. Environ. Monit. 14, 3156-3163.

Tables

Table 1: Percent contribution for the different POP groups to the summed measured burden in five sampling years for 53 Norwegian men in the Tromsø Study based on the data reported in Nøst et al. (2013; 2014).

Compounds[a]	**1979**	**1986**	**1994**	**2001**	**2007**
$\Sigma HCHs_3$	2	1	0	0	0
$\Sigma DDTs_5$	26	12	5	3	3
HCB	4	2	1	1	1
$\Sigma chlordanes_5$	2	2	1	1	1
$\Sigma toxaphenes_2$	1	1	0	0	0
$\Sigma PCBs_{24}$	30	19	12	9	9
PFOS	20	36	45	51	52
Σother $PFASs_8$	16	27	35	34	33

[a]$\sum$ signifies the summed concentrations in each group and the subscript the number of compounds in each group.

Figure legends

Figure 1.

Wet-weight concentrations of PCBs, OCPs, and PFASs from 1979 to 2007 for 53 men based on the data reported in Nøst et al. (2013; 2014; reproduced with permission from *Environmental Health Perspectives* and *Environment International*) for repeated measurements of men in the Tromsø Study. PFOS represents the sum of linear and branched forms. See Table 1 for the number of compounds in each sum.

Figure 2.

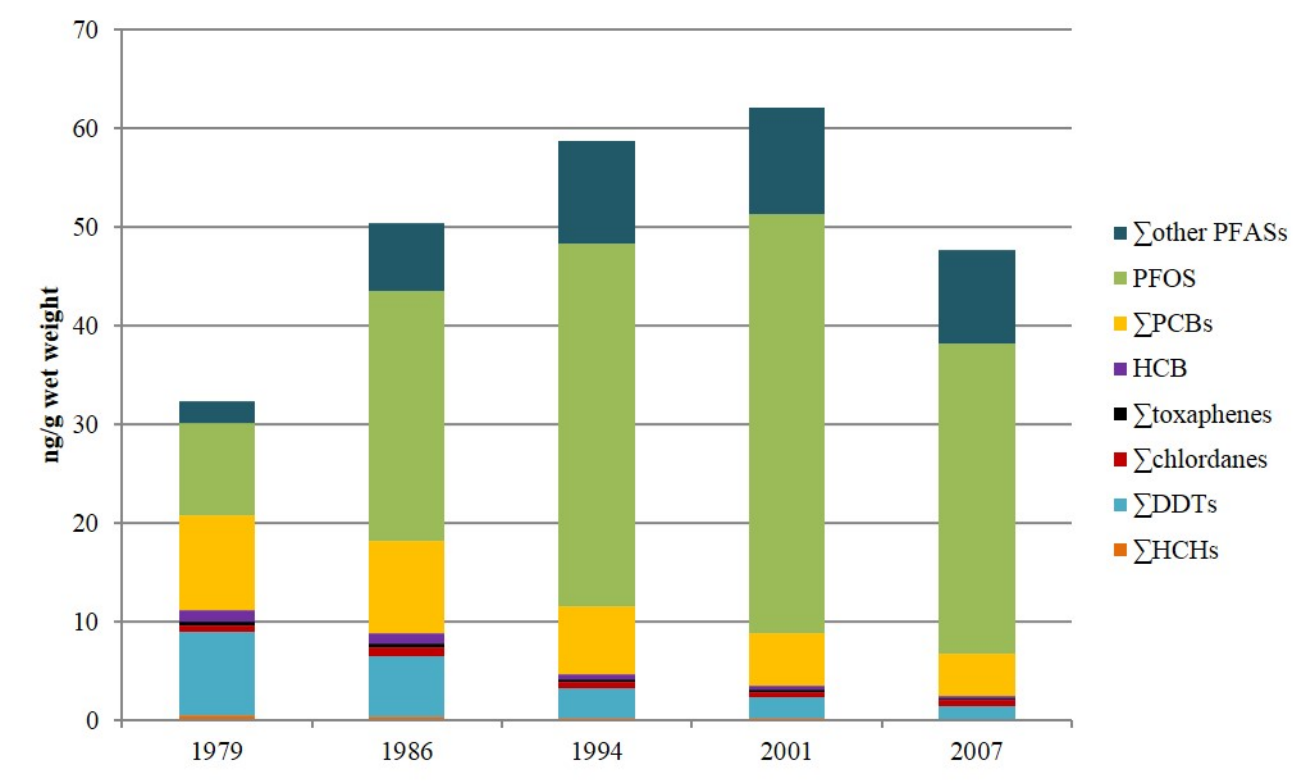
The horizontal axes represent calendar years, left vertical axes the emissions/production volumes in thousands tons (colored areas), and right vertical axes the wet-weight serum concentrations in the five repeated measurements from Norwegian men (bars; n=53). A: Estimated regional emissions for PCB-153 from 1930 to 2020 (adapted from Breivik et al., 2007) are displayed along with the measured serum concentrations of PCB-153. B: Estimated global emissions of DDT from 1941 to 2005 adapted with permission from Schenker et al., (2008; Copyright American Chemical Society) conjointly with the serum concentrations of *p,p′*-DDT. C: Estimated global production volumes of the PFOS-related perfluorooctanesulfonyl fluorides from 1970 to 2005 (adapted with permission from Paul et al., 2009; Copyright American Chemical Society) are shown along with the serum concentrations of PFOS (sum of linear and branched).

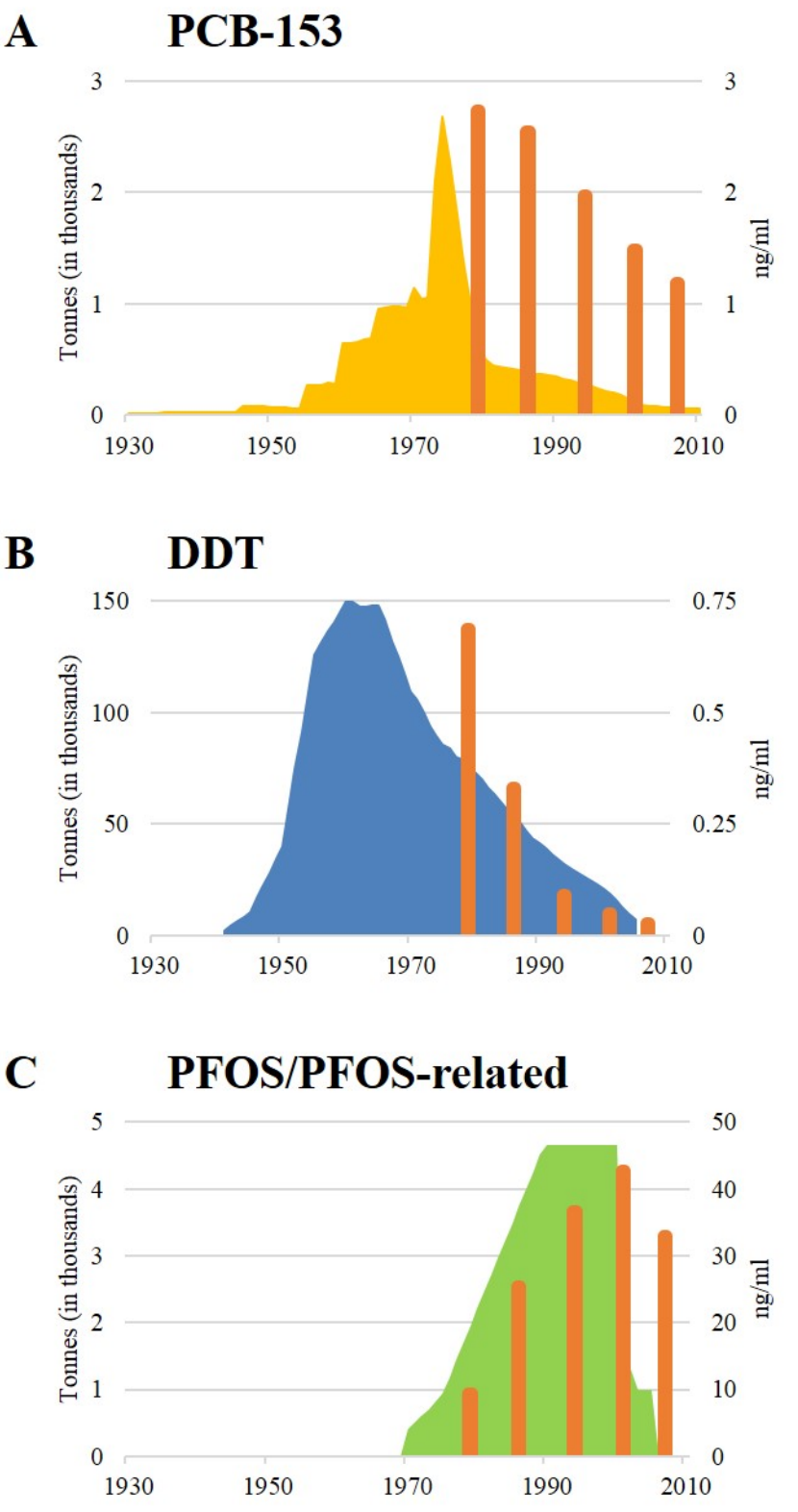
Figure 3.

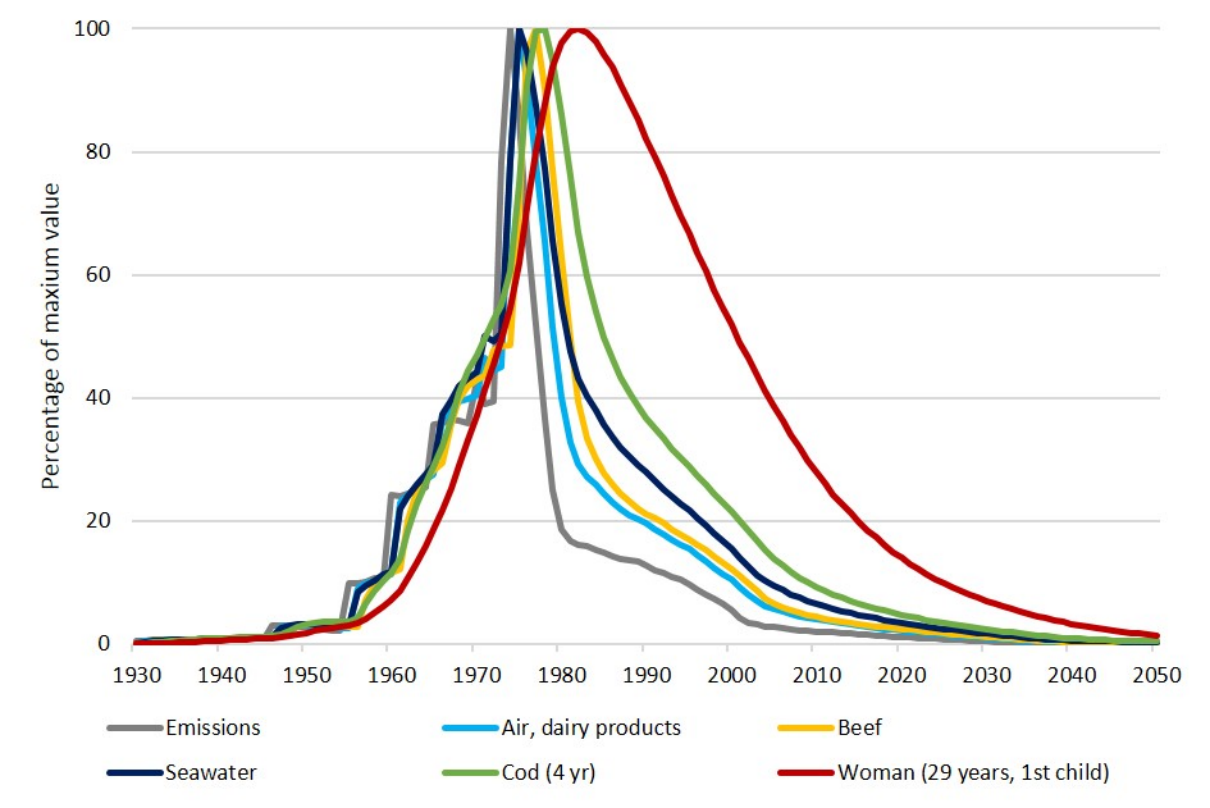
Estimated trends in emissions and concentrations from 1930 to 2050 for PCB 153 scaled to the maximum value for each medium. Note that the trends for air and dairy products overlap and are presented as one line. The plotted curve for the 29-year old woman refers to blood concentrations after

434 nursing her first child for 6 months. Further details of the model parameterization are presented in

435 Breivik et al. (2010) and references therein, and as later explored by Nøst et al (2013).


70
60
50
40
30
20
10
0
ng/g wet weight
1979
1986
1994
2001
2007
∑other PFASs
PFOS
∑PCBs
HCB
∑toxaphenes
∑chlordanes
∑DDTs
∑HCHs


A
PCB-153
Tonnes (in thousands)
ng/ml
0
1
2
3
1930
1950
1970
1990
2010
B
DDT
Tonnes (in thousands)
ng/ml
0
50
100
150
0
0.25
0.5
0.75
1930
1950
1970
1990
2010
C
PFOS/PFOS-related
Tonnes (in thousands)
ng/ml
0
1
2
3
4
5
0
10
20
30
40
50
1930
1950
1970
1990
2010


Percentage of maxium value
100
80
60
40
20
0
1930
1940
1950
1960
1970
1980
1990
2000
2010
2020
2030
2040
2050
Emissions
Air, dairy products
Beef
Seawater
Cod (4 yr)
Woman (29 years, 1st child)