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Human biomonitoring of perfluoroalkyl substances and cyclic volatile methylsiloxanes

Concentrations in plasma, serum and whole blood from pregnant, delivering or postmenopausal women, and cord blood

Linda Hanssen

A dissertation for the degree of
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Preface/Acknowledgement

This voyage started 13 years after I had completed my master in organic chemistry. In 2006, when taking a course at University of Tromsø, I realized that it is never too late to learn something new, and began looking for available PhD positions. One of the course lecturers was Jon Øyvind Odland, enthusiastic as always about the importance and impact of environmental contaminants on human health. Within a year I became one of his students. Torkjel Manning Sandanger also became involved in the project together with Evert Nieboer. You three together are a great team with different qualities that complement each other. I once called Jon Øyvind a "godfather": he is present in the background, provides the overview, as well as enthusiasm and encouragement. I had just started my PhD and heard a rumour about you Evert, and it is true. If you want something well written, he is the man. I am very grateful for your knowledge and contribution. Torkjel: positive, funny, energetic, caring, smart and intense, these are just a few words that describe you. You have inspired me, encouraged me, and I am very grateful for your guidance through my PhD.

This thesis would not have been completed without the other co-authors of the three paper: Tonje Braathen for statistics; Morten K. Moe for insight in the world of LCMS; Alexey A. Dudarev for fast responses on strange questions about Russia; Eiliv Lund for letting me include the NOWAC samples (you are a great epidemiologist); Halina Röllin (you are a true lady), I am grateful that I had the opportunity to visit you and Kala in South Africa, and for the glimpse of your magnificent country; the "MISA gang": Solrunn, Anna-Sofia and Bente for your help in getting the MISA samples; and Ole-Anders Braathen for providing some extra income and a job so that I could continue working on the thesis until the end.

Formally I was associated with the Department of Community Medicine at the University of Tromsø. Being part of the first class of the EPINOR research school meant that a chemist had to learn a lot about epidemiology and related statistics in addition to conquering STATA. To what degree I have succeeded, I am not the judge; nevertheless, it has been fun. I have also enjoyed teaching medical students the significance of epidemiology and statistics. An important part of the EPINOR class has been Laila and Anita. Thank you for always letting me feel included, even though my visits were rare. This was due to the fact that my work place was located at NILU's Fram Centre.

The work presented was carried out at NILU. The chemists there are among the best in the World! Eldbjørg you are very warm hearted and inclusive. You welcome every new student

and make room for each. You are a “Marte Svennerud” (ittno knussel, je tar dom alle). Thank you Sandra for always having time to answer questions, helping me with instruments and standards, and showing me how to handle LCMS instruments. It was a new world for a GCMS girl! Dorte, you are a living PFAS Wikipedia; for a Google girl this meant a lot. Nick, your enthusiasm, help and guidance into the world of siloxanes were very much appreciated. Therese without your open door and willingness to listen when I was talking to myself the road would have been more difficult. Lotta (aka Fr Rylander), the brain behind the CSI movie, you made sure not to forget that fun is an important part of life. Remember the lions in the Kruger Park at night?

My appreciation is also extended to others: Colleagues at NILU in Tromsø for the cake and coffee breaks; people at NILU-Kjeller for helping me during my visits with equipment–with special thanks to Heriette Leknes and Ingjerd Sunde Krogseth for taking care of the instruments during the siloxane analyses; and the delivering, pregnant and post-menopausal women study participants, who donated blood samples and completed questionnaires. Without them this project would not have been possible.

And then My mum, who lives by the expression: “It is never too late to learn something new”.

And above all my family. When you, my dear husband, encouraged me to start on my PhD, did you know what it meant? I am finally done! My children that have watched mum working, and picked up some new “strange” words (PFOS and siloxanes etc.). You make me proud!

Summary

In human biomonitoring (HBM) of exposure, concentrations of xenobiotic compounds are measured in biological tissues. We have investigated two groups of emerging contaminants with different source of exposure namely, perfluoroalkyl subtances (PFASs) and cyclic volatile methylsiloxanes (cVMS). PFASs are ubiquitous in the environment world-wide, and cVMS are present as constituents in many personal care products (PCPs). The primary exposure route for PFASs is the diet, whereas dermal application of PCPs is so for cVMS. In terms of persistence, the human half-life for PFASs is several years, while for cVMS it is two to three days.

Our primary objective for PFASs was to assess exposure in blood in delivering women and their new-born residing in countries for which this information was lacking, specifically: South Africa, the industrial city of Norilsk (arctic Russia) and the rural Aral Sea region of Uzbekistan. A secondary objective was to evaluate the distribution of PFASs between blood cell and plasma fractions. In terms of cVMS, we wanted to evaluate if they were present in blood plasma of pregnant and postmenopausal Norwegian women, and to investigate possible links to self-reported use of PCPs for the latter group.

The PFAS concentrations in delivering women were highest in arctic Russia followed by South Africa and Uzbekistan. Put in context with other studies, year of sampling and geographical location were main predictors for PFASs exposure. Even though plasma and serum are the biological tissue most often used in HBM studies, we observed that whole blood contained considerably amount of a perfluorooctane sulfonic acid (PFOS) precursor, namely perfluorooctane sulfonamide (FOSA). Compared to PFOS and other "ionic" PFASs, reporting FOSA concentrations in plasma (or serum) results in an underestimation of exposure. Specifically, the concentration in whole blood was up to six times higher than in plasma. The rather basic pK_a value of FOSA appears to explain this difference in distribution.

The majority of the women had paired umbilical cord samples, and the presence of PFASs in these samples showed that the unborn child is also exposed to these compounds. When comparing concentrations of compounds with the same number of backbone carbons in maternal and cord plasma and whole blood, the data suggest that a perfluoroalkyl carboxylic acid (PFCA) passes the placenta more easily than the corresponding perfluoroalkyl sulfonic acid (PFSA).

The ubiquitous presence of cVMS in the general environment make their analysis challenging. Several novel actions were implemented to minimize inadvertent contamination. The plasma cVMS concentrations reported are the first for women from the general population. Information about PCP used was not significant correlated with cVMS concentration. It should be pointed out that even though the majority of the investigated cVMS were present below the detection limit, the concentrations that were found were still substantial compared to those for prominent persistent organic pollutants (POPs). For example, the Limit of quantification (LOQs) for the cVMS were three times the currently reported concentration of PCB 153, a compound we still are concerned about. The cVMS add to the mixture of xenobiotic compounds in human blood and thus contribute to the complex and concerning cocktail of contaminants.

Sammendrag

Mennesker eksponeres for en rekke miljøgifter gjennom diett og ved bruk av produkter som er ment til å forbedre hverdagen. I human overvåkning (HBM) kartlegges mengden fremmedstoffer i kroppen.

Vi har undersøkt to grupper fremmedstoffer som betegnes som nye; perfluoralkyl forbindelser (PFASs) og sykliske siloksaner (cVMS). Kildene til den humane eksponeringen for disse forbindelsene er ulike. PFASs er utbredt i miljøet over hele verden, og cVMS er tilstede, i varierende mengder, i mange typer hudpleie produkter. For PFASs er hovedeksponeringen via mat mens for cVMS er påføring/bruk av hudpleie produkter en kilde. Disse to gruppene av fremmedstoffer har ulik persistens (levetid i miljøet og mennesket) der den humane halveringstiden for PFASs flere år, mens for siloksaner er den under en uke.

Vårt primære mål var å undersøke eksponeringen til disse stoffene, det vil si mengden PFASs i blodet til fødende kvinner og deres nyfødte barn (navlestrengsblod) bosatt i land der denne informasjonen var mangelfull; Sør Afrika, Norilsk (industriby i arktiske strøk av Russland) og landsbygda nær Aral sjøen i Usbekistan. Et sekundært mål var å se på fordelingen av PFASs mellom blodcellene og plasma i mor og navlestrengsblod. For cVMS ønsket vi å se om de var tilstede i blodet til gravide og postmenopausale kvinner fra Norge, og videre undersøke om det var en sammenheng mellom konsentrasjonene og bruk av hudpleieprodukter i den siste gruppen.

PFAS konsentrasjonen i de fødende kvinnene var høyest i arktiske strøk av Russland etterfulgt av Sør Afrika og Usbekistan. Konsentrasjonene var generelt lavere enn i den vestlige verden. Sammenligning med andre studier viste at innsamlingsår og geografisk lokalisering var hovedprediktorer for den målte PFASs konsentrasjonen. Selv om plasma og serum er de biologiske væskene oftest brukt i HBM studier, observerte vi at fullblod inneholdt betydelige mengder av en forløper til perfluoroktansulfonat (PFOS), perfluoroktansulfonamid (FOSA). Sammenlignet med PFOS og andre «ioniske» PFASs, har eksponeringen til FOSA i tidligere studier vært underestimert når plasma/serum har vært undersøkt. Konsentrasjonen av FOSA i fullblod var opptil seks ganger høyere sammenlignet med plasma. Den høye pK_a verdien for FOSA, hvor FOSA ikke er fullstendig dissosiert ved fysiologisk pH, sammenlignet med andre PFASs kan forklare denne forskjellen i distribusjon.

For majoriteten av kvinner hadde vi navlestrengsblod tilgjengelig, og tilstedeværelsen av PFASs i disse prøvene viser at det ufødte barnet er eksponert for disse forbindelsene. Ved sammenligning av konsentrasjonene til forbindelser med lik kjedelengde av den fluorerte karbonkjeden, fant vi at perfluoralkylkarboksylater (PFCA) passerer placenta lettere enn den korresponderende perfluoralkylsulfonaten (PFSA).

Der hvor mennesker oppholder seg er det også cVMS er tilstede, og analysen av disse forbindelsene er derfor utfordrende. Flere tiltak ble gjennomført slik at kontaminering fra mulige kilder ble minimert. For første gang er cVMS rapportert i plasmaprøver fra en populasjonsbasert kohorte. Mengden cVMS varierte fra ikke detektert til 12.7 ng/mL. Informasjon om PCP bruk var ikke signifikant korrelert med målt cVMS konsentrasjon. Det må bemerkes at selv om majoriteten av de undersøkte cVMSene var under deteksjonsgrensen, var konsentrasjonen betydelig sammenlignet med de kjente miljøgiftene slik som polyklorerte bifenyler (PCB). For eksempel er kvantifiseringsgrensen (LOQ) for cVMS tre ganger høyere enn konsentrasjoner nylig rapportert for PCB 153, en forbindelse man fortsatt er bekymret for. cVMS kan legges til den allerede kjente listen av miljøgifter i blodet og bidra til den omtalte «cocktail» effekten.

TABLE OF CONTENT

LIST OF PAPERS

This thesis is based on three papers referred to in the text by their Roman numerals.

I. **Perfluorinated compounds in maternal serum and cord blood from selected areas of South Africa: results of a pilot study.** Hanssen L, Rollin H, Odland JØ, Moe MK, Sandanger TM, J Environ Monit. 2010; 12: 1355–1361.

II. **Partition of perfluoroalkyl substances (PFASs) in whole blood and plasma, assessed in maternal and umbilical cord samples from inhabitants of arctic Russia and Uzbekistan.** Hanssen L, Dudarev AA, Huber S, Odland JØ, Nieboer E, Sandanger TM. Sci Total Environ. 2013 ;447:430-437

III. **Plasma concentrations of cyclic volatile methylsiloxanes (CVMS) in pregnant and postmenopausal Norwegian women and self-reported use of personal care products (PCPs)**. Hanssen L, Warner NA, Braathen T, Lund E, Odland JØ, Nieboer E, Sandanger TM. Environ Int. 2013; 51: 82-87.

ABBREVIATIONS

AMAP	Arctic Monitoring and Assessment Programme
BFRs	Brominated flame retardants
cVMS	Cyclic volatile methylsiloxanes
D4	Octamethylcyclotetrasiloxane
D5	Decamethylcyclopentasiloxane
D6	Dodecametylcyclohexasiloxane
ECF	Electrochemical fluorination
FOSA	Perfluorooctane sulfonamide
FTOH	Fluorotelomer alcohol
HBM	Human biomonitoring
LC-QToF	Liquid chromatography Quadrapole–time of flight
LOD	Limit of detection
LOQ	Limit of quantification
LRT	Long range transport
MISA	Miljøgifter i Svangerskapet og Ammeperioden (North Norwegian Mother-and-Child Study)
MDL	Method detection limit
NILU	Norwegian Institute for Air Research
NOAEL	No observed adverse effect level
NOWAC	Norwegian Women and Cancer Study
PBDE	Polybrominated diphenyl ether
PCB	Polychlorinated biphenyl
PCP	Personal care product
PFAS	Perfluoroalkyl or polyfluoroalkyl substance
PFBA	Perfluorobutanoic acid

PFCA	Perfluoroalkyl carboxylic acid
PFHxA	Perfluorohexanoic acid
PFHxS	Perfluorohexane sulfonic acid
PFOA	Perfluorooctanoic acid
PFOS	Perfluorooctane sulfonic acid
PFNA	Perfluorononanoic acid
PFDA	Perfluorodecanoic acid
PFDoDA	Perfluorododecanoic acid
PFPA	Perfluorinated phosphonic acids
PFSA	Perfluoroalkyl sulfonic acid
PFUnDA	Perfluoroundecanoic acid
POPs	Persistent organic pollutants
POSF	Perfluorooctane sulfonyl fluoride
PPAR	Peroxisome proliferator activated receptor
p,p´-DDE	*p,p´*-dichlorodiphenyl dichloroethene
RBC	Red blood cell
SRM	Standard reference material
UCB	Umbilical cord blood
UPLC-MS-MS	Ultra high pressure liquid chromatography triple-quadrupole mass-spectrometry

1. INTRODUCTION

1.1 PREAMBLE

The general population is exposed daily to a wide range of anthropogenic compounds through the diet and the handling of consumer products meant to improve everyday life. Several of them have been shown to have adverse effects both in the environment and in humans. The legacy POPs (persistent organic pollutants), such as organochlorine pesticides and polychlorinated biphenyls (PCBs) (see Figure 1 for structural details) have been of special interest. They biomagnify, are persistent in the environment (long half-lives) and undergo long range transport (LRT) (AMAP, 2003; 2004a). International agreements, such as the Stockholm Convention on POPs, have resulted in restricted production and use. As a result, the concentration of these compounds has decreased over time in the environment and so has the exposure of the general human population. More recently, other organic contaminants are being identified as being widely distributed. Examples are brominated flame retardants (BFRs), perfluoroalkyl and polyfluoroalkyl substances (PFASs) and silicones (see Figure 1). They are designated as emerging contaminants even though they have been commercially available, since the beginning of the 1970s, 1950s and 1940s (Prevedouros et al., 2004; Paul et al., 2009; Wang et al., 2012), respectively. At the beginning of the 21st century, improved analytical equipment and techniques confirmed the presence of PFASs in human serum and the general environment world-wide (Giesy and Kannan, 2001; Hansen et al., 2001). To circumvent similar delayed environmental contamination legacies, model-based tools are used today. The silicones (more specifically cyclic volatile methylsiloxanes; cVMS) constitute a concern because of their predicted persistence, bioaccumulative characteristics and high production volume (Howard and Muir, 2010; Warner et al., 2010; Kierkegaard et al., 2011).

The research described in this thesis focuses on human biomonitoring (HBM) aspects of PFASs and cVMS.

1.2 PRODUCTION AND USE

1.2.1 Perfluoroalkyl[a] and polyfluoroalkyl[b] substances (PFASs)

PFASs have been produced since 1949 and, as mentioned, were commercially available shortly thereafter (Prevedouros et al., 2006; Paul et al., 2009). As illustrated in Figure 1, a PFAS consists of a hydrophobic fully fluorinated alkyl chain and a hydrophilic functional group. These chemical/structural features confer PFASs unique properties including: being "chemically inert, non-wetting, very slippery, non-stick, highly fire resistant, very high-temperature ratings, and highly weather resistant", and initially they were considered as nontoxic (Herzke et al., 2012). The major commercial uses of PFASs has been as raw materials for surfactant and surface protection products, but also as components of: inks, varnishes, waxes, fire fighting foams, metal plating and cleanings, coating formulations, lubricants, water and oil repellents for leather, paper and textiles, and insecticide (Butenhoff et al., 2006; Paul et al., 2009; Buck et al., 2011).

[a]Perfluoroalkyl compounds: All of the hydrogen in the alkyl chain have been substituted with fluorine (e.g., Perfluorooctanoic acid; PFOA).

[b]Polyfluoroalkyl compounds: Some of the hydrogen in the alkyl chain have been substituted with fluorine (e.g., fluoropolymers).

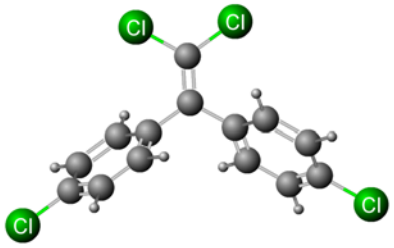
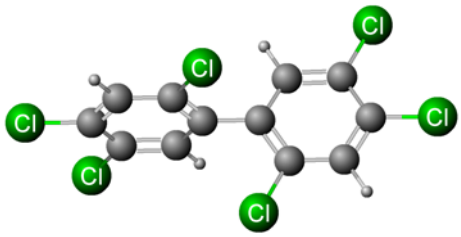
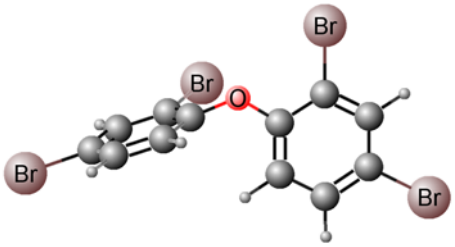
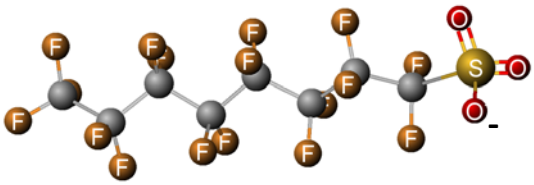
Compound	Structure
p,p'-DDE (a legacy POP)	
PCB 153 (a legacy POP)	
PBDE 47 (a BFR)	
PFOS (a PFAS)	
D5 (a cVMS)	

Figure 1. Chemical structures of *p,p'*-DDE (*p,p'*-dichlorodiphenyl dichloroethene), PCB 153, PBDE (polybrominated diphenyl ether) 47, PFOS (perfluorooctane sulfonic acid) and D5 (decametylcyclopentasiloxane). (Illustrations by E.S. Heimstad)

Two main production processes have been employed in the production of PFASs, namely electrochemical fluorination (ECF) and telomerisation (see Figure 2). Until 2002, the 3M Company (3M) was the major global manufacturer of perfluorooctane sulfonyl fluoride (POSF) using the ECF production method (see Figure 3) (Paul et al., 2009). During this process, an impure mixture of linear and branched isomers and chain-length homologs are formed (Lau et al., 2007; Benskin et al., 2009a). POSF and salts of perfluorooctanoic acid (PFOA) were the main products. POSF served as a building block in the synthesis of high molecular weight fluorochemical products, and the ammonium salt of PFOA in the manufacture of fluoropolymers (Buck et al., 2011). POSF-based derivatives served as major raw materials for surfactants and surface protection products and included the following neutral volatile compounds: *N*-methyl perfluorooctane sulfonamidoethanol (MeFOSE), *N*-ethyl perfluorooctane sulfonamidoethanol (EtFOSE), *N*-Methyl perfluorooctane sulfonamide (MeFOSA), and *N*-Ethyl perfluorooctane sulfonamide (EtFOSA) (Buck et al., 2011). Perfluorooctane sulfonic acid (PFOS) was produced in minor quantities (Paul et al., 2009). In total, 96 000 tonnes of POSF were produced (Paul et al., 2009). The estimated global POSF production volume from 1970-2002 is presented in Figure 3.

Perfluoroalkyl carboxylic acids (PFCAs), fluorotelomer alcohols (FTOHs), fluorotelomer iodides and fluorotelomer olefins were among the products of the telomerisation process, which have been used by various companies since the 1970s (Butt et al., 2010). These compounds were used as building blocks in the synthesis of polyfluorinated polymers for use as ingredients of textile treatment surfactants, and grease-proof food contact paper (Buck et al., 2011; Lindstrom et al., 2011). Unlike the ECF process, telomerisation leads to a homologous series of linear perfluoroalkyl chains with even-numbered carbon chain-lengths (Martin et al., 2005; Buck et al., 2011).

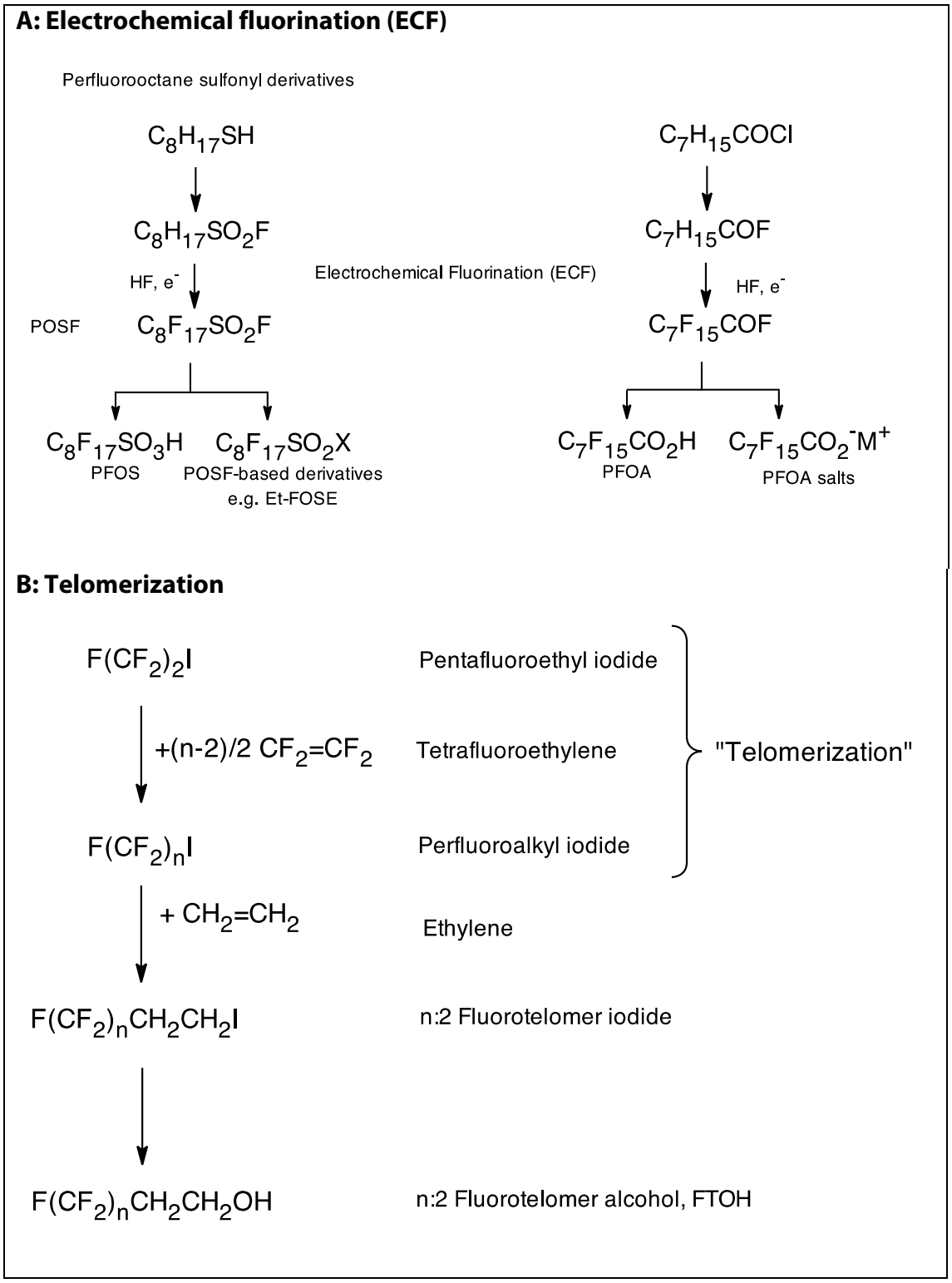


Figure 2. Simplified description of the ECF (A) and telomerization (B) processes (adapted from Buck et al., 2011).

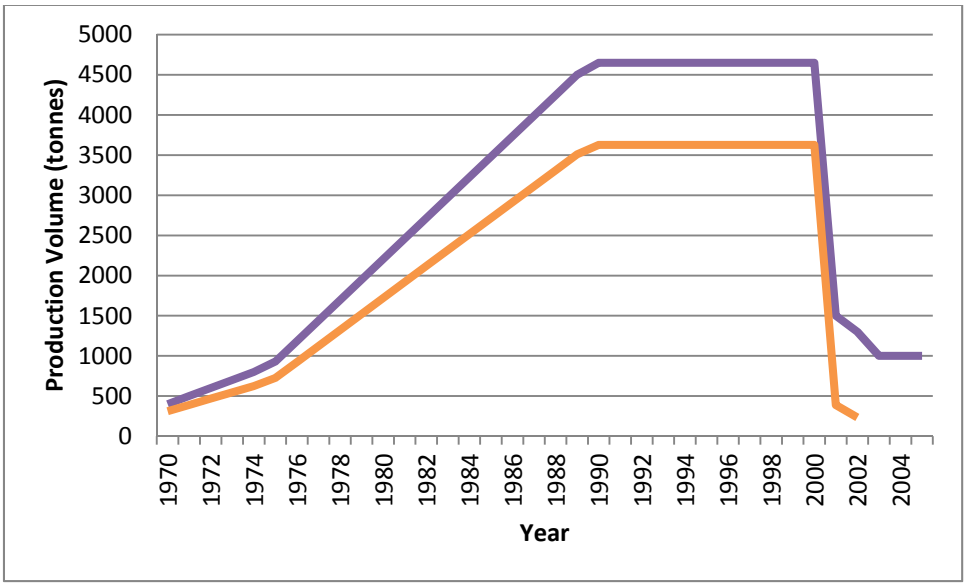


Figure 3. Estimated global POSF production volume (1970-2002), purple line; 3M's production, orange line (adapted from Paul et al., 2009).

1.2.2 Cyclic volatile methylsiloxanes (cVMS)

Siloxanes (also known as organosiloxanes; Brooke et al., 2009a-c) are widely used chemicals and constitute the building blocks of silicone products. Silicones exhibit high thermo stability, chemical resistance, inertness and good lubrication properties, and have been used as an alternative to PCBs (Dow Corning, 2004). While the stability of silicones are desirable from a technical point of view, it renders them environmentally persistent. Silicones on treated polymers serve as an alternative to fluorinated chemicals since they offer good water repellency (Posner, 2012), and are used in a number of industrial applications and consumer products (Kaj et al., 2005a; Horii and Kannan, 2008; Wang et al., 2009).

Productions of silicones are carried out primarily in the USA, Germany, Japan, France and the U.K. (Lassen et al., 2005). However, China has become the largest manufacturer and consumer of polysiloxanes in the world (Wang et al., 2012). Globally the use of silicones sums to 850 000 tonnes (Lassen et al., 2005). The production volume estimates for 2006 covered quite a range: 45 000 - 227 000 tonnes (octamethylcyclotetrasiloxane; D4) and 23 000 – 45 000 tonnes (decamethylcyclopentasiloxane; D5) (Howard and Muir, 2010). Recent numbers from China indicate that the output of polysiloxanes for 2008 and 2009 was 195 000 and 270 000 tons, respectively (Wang et al., 2012). According to the database on the use of *Substances in Products in the Nordic Countries* (it is based on data from the Product

Registries of Norway, Sweden, Denmark and Finland), the registered use of D4, D5 and D6 (dodecamethylcyclohexasiloxane) in substances, and have in Norway have decreased since 2004 (see Figure 4). However, the declaration of cVMS in personal care products (PCPs) is not mandatory in Norway (Huse and Aas-Aune, 2009), and therefore not included in this figure.

There are five major groups of organosiloxanes: oligomeric organosiloxanes (also known as the volatile methyl siloxanes); polymeric dimethylsiloxanes, modified polymeric dimethylsiloxanes, organosiloxane resins and organosiloxane elastomers. Of the latter four categories (organosiloxane resins exempted), all could contain traces of cVMS, specifically: D4, D5 (see Figure 1 for chemical structure) and D6. Oligomeric organosiloxanes (especially D4 and D5) are used in PCPs, specifically as carriers in antiperspirants, deodorants, skin care products, and as conditioners in hair care products. To enhance skin smoothness and softness when using PCPs, siloxanes are added to cosmetic lotions as emollients (moisturizers) (Brooke et al., 2009a-c). Other properties, such as the high volatility of cVMS, are desirable since most of that applied evaporates from the skin within 24 h (Reddy et al., 2007). In addition to PCPs, siloxanes are used in a number of industrial applications and in consumer products including: fuels, car polishes, cleaners, anti-foaming agents, and car waxes (Lassen et al, 2005).

The numerous applications of cVMS, and especially their high volatility, have raised concern about these compounds within environmental science disciplines (Kaj et al., 2005a). D5 is currently being subjected to regulatory scrutiny, including the suggestion that it should be classified as a “very persistent and bioaccumulative substance” (Brooke et al., 2009b).

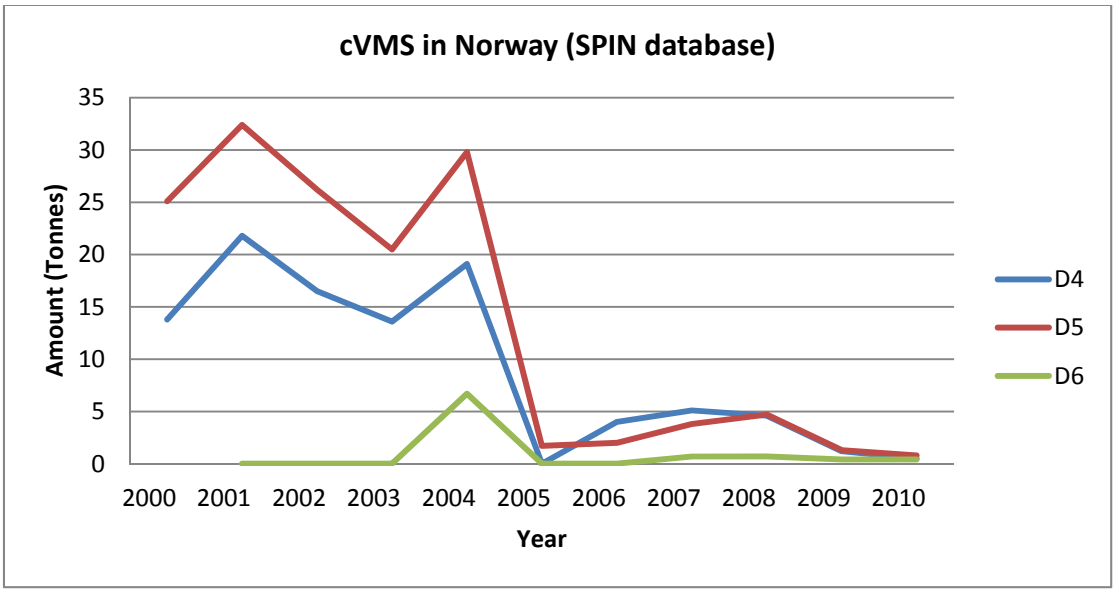


Figure 4. Tonnes of cVMS in Norway registered used in the SPIN database (SPIN, 2012).

1.3 Sources and Environmental Distribution

1.3.1 PFASs

PFASs were perceived to be biologically inert primarily because of their incorporation into polymers (Giesy and Kannan, 2001). On this basis, they were believed to have little impact on the environment, including human health.

They are known to be released into air, water and land during their manufacture and v*ia* secondary products such as fire fighting foams and their presence in consumer products. They have been detected in a variety of environmental matrices such as air, surface water, sludge, soil, sediments, and ice caps (Lau et al., 2007). The highest environmental concentrations have been reported for the northern hemisphere (Jahnke et al., 2007; Ahrens et al., 2009), where the majority of the PFAS production has taken place (OECD, 2002). However, there has been some limited production in Brazil (Danish EPA, 2005). Concentrations in various air and water indicate limited mass exchange of PFASs between the two hemispheres (Jurado et al., 2004).

The relatively long half-life in air of 10-20 days and ability to undergo LRT of the precursors to PFOS and PFOA, namely FOSEs, FOSAs and FTOHs, potentially permits transport to remote regions such as the Arctic. When these precursors undergo abiotic or biotic

degradation (biotransformation), PFOS and PFOA are the major end products. The latter are stable compounds with no known natural degradation pathways (Ellis et al., 2004; Plumlee et al., 2009; Martin et al., 2010; Buck et al., 2011; Lindstrom et al., 2011). Another transport pathway is by water, which would be more relevant for the ionic compounds of PFCA and perfluoroalkyl sulfonic acids (PFSAs).

Long chain PFSAs and PFCAs with eight carbon atoms or more in the fluorinated chain accumulate significantly in the food chain (Conder et al., 2008). This implies that PFOS (8 carbons) bioaccumulates and PFOA (7 carbons) has a lower potential to do so (Butt et al., 2010); nevertheless, both compounds are environmentally persistent. In 2009 PFOS was included in Annex B of the Stockholm Convention, which restricts its use and production (UNEP, 2011).

1.3.2 cVMS

Release from industrial processes related to the production and use of silicone polymers and disposal of PCPs are the primary environmental sources of cVMS (Environment Canada and Health Canada, 2008 a-c). More than 90% are released to the atmosphere and the remainder is discharged to waste water (Genualdi et al., 2011). cVMS are eliminated from the atmosphere largely by reactions with OH• to form silanols, which are scavenged by wet deposition. Neither wet nor dry depositions of the native cVMS are expected (McLachlan et al., 2010). The half-lives in the atmosphere of D4 and D5 are approximately 15 and 10 days respectively, and are sufficiently long to undergo LRT to remote regions such as the Arctic (McLachlan et al., 2010).

cVMS have been detected in matrices including air, water, sediments, fish and birds, even in the Arctic (Sparham et al., 2008; Evenset et al., 2009; McLachlan et al., 2010; Warner et al., 2010; Sparham et al., 2011). The highest concentrations in water and sediments are found close to effluent sources. Air samples are dominated by D5 and D6 near cities, whereas in D3 and D4 dominate in remote locations (Genualdi et al., 2011). Surface water concentrations of cVMS reflect their divergent solubilities in this medium. In other environmental samples, concentrations of D5 have often exceeded those of D4 and D6 (Warner et al., 2010). This mirrors the larger production of D5 (in Europe) compared to D4 (Wang et al., 2012).

On release, the residence time in air of D5 is 2.9 days and, based on model simulations, is considerably longer in water (estimated at 201 days; Hughes et al., 2012). The latter implies distribution to the water column and sediments. A more realistic scenario with respective releases of 94.5%, 0.8% and 4.7% D5 into air, water and soil, respectively, gave and overall residence time in the environment of 4.6 days. A trophic magnification factor (TMF) significantly greater than one has been reported for D5 (Borgå et al., 2012), suggesting food web biomagnification. On the other hand two other studies suggest TMF<1 (Powell et al., 2009; 2010).

1.4 HUMAN BIOMONITORING OF EXPOSURE

1.4.1 Preamble

*"Human biomonitoring (HBM) involves the monitoring of dose, effect and susceptibility in body fluids or tissues (Nieboer et al., 1999; WHO, 1993)**. A biomarker of exposure** is "the environmental contaminant, its metabolite, or a product resulting from its interaction with the target tissue"; **a biomarker of effect** corresponds to "a measurable biochemical, physiological behavioural or other alteration within an organism that, depending upon the magnitude, can be recognized as associated with an established or possible health impairment or disease"; and **a biomarker of susceptibility** is "an indicator of an inherent or acquired ability of an organism to respond to the challenge of exposure to a specific xenobiotic substance" (WHO, 1993). Exposure biomarkers are assessed through measuring the presence and concentration of chemicals in blood, urine, hair, nails or breath (exhaled air)"* (Odland and Nieboer, 2012). Of course other tissues can also be used, such as breast milk meconium, saliva, sweat, and semen (Esteban and Castano, 2009). Clearly, the work described in this thesis is limited to biomarkers of exposure in body fluids, namely plasma, serum and whole blood.

Specimens collected from pregnant and delivering women, namely blood (whole blood, serum, or plasma) and breast milk, have been used as biomarkers of fetal and/or neonatal exposure. The ability to cross the placenta varies, with the majority of contaminants doing so and thereby entering the fetal circulation. Another common way of assessing fetal exposure involves analysing cord blood at birth. Amniotic fluid and meconium also have received attention for this purpose (Barr et al., 2005; Jensen et al., 2012). The half-life of

xenobiotics in meconium may be protracted, and thus measured concentration of contaminants may reflect cumulative exposure from the second trimester to delivery (Whyatt et al., 2009).

1.4.2 PFASs

Since 2001 there have been several reports on PFAS concentrations in the general population. Whole blood, serum and plasma have been used as sample matrices to determine the internal exposure. However the majority of the studies have reported PFAS concentrations for the latter two (Lau et al., 2007; Martin et al., 2010). A likely reason is that they are preferred matrixes from the analytical perspective, are routinely used in clinical chemistry (Burtis et al., 2006), and have often been collected for storage in bio-banks. The PFAS concentrations in plasma and serum have shown to be comparable, although there have been some uncertainties when whole blood concentrations have been compared with plasma and serum concentrations. It has generally been assumed that concentrations in serum and plasma measurements would be approximately twice that in whole blood because of its cellular components (Kannan et al., 2004; Kärrman et al., 2006). This has shown to be valid for ionic PFASs such as PFOS and PFOA (Ehresman et al., 2007), although the plasma-to-whole blood ratio for FOSA has been reported to be 0.2 (Kärrman et al., 2006). In contrast to POPs, only minor amounts of PFASs appear stored in the lipids (Jones et al., 2003). The question of the proper media for PFAS measurements remains unresolved. In recent animal studies, whole blood has been the preferred sample matrix to determine the internal exposure to some PFASs (D'eon and Mabury, 2010; Ross et al., 2012).

Exposure to contaminants usually decreases in the order: occupational exposure > populations with identified local exposure sources (including LRT) > the general population (i.e., background exposure). Biomonitoring studies of workers involved in the production of PFAS, or the manufacture of products containing them, have shown serum concentrations exceeding 10 000 µg/L (PFOS) and > 100 000 µg/L (PFOA) (Fromme et al., 2009). Recently, elevated exposure to PFASs among ski waxing technicians has been reported (Nilsson et al., 2010). Among populations with identified local exposure sources (e.g., in Sauerland, North Rhine-Westphalia, Germany and Little Hocking, Ohio, USA), PFASs have been detected in the municipal drinking water, with PFOA the most prominent compound found (Fromme et al., 2009; Steenland et al., 2009). LTR appears to contribute to PFAS exposures of indigenous peoples living at northern latitudes (local food is a source) (Ostertag et al.,

2009; Donaldson et al., 2010). In the general population, diet has been considered the major exposure pathway for PFASs (including food packaging materials) (Fromme et al., 2009; Domingo, 2012). By analogy to brominated compounds (e.g., PBDEs), house dust may well constitute an exposure source. PBDEs are ubiquitous in household products (including common food items, upholstery, textiles, building materials, kitchen appliances, plastic products and electronics). This exposure pathway has been shown to be significant, especially for toddlers who ingest more dust than adults (Frederiksen et al., 2009; 2010). Indeed, house dust also appears to contribute to PFASs exposure (Domingo, 2012) for which the concentrations of PFAS precursors are often higher than the ionic PFASs (Haug et al., 2011).

The measurement of contaminants in exposure media such as air, house dust, drinking water and foods allows intake doses to be calculated. Which of these exposure sources dominates depends on the type of compound and the uptake route. Several studies have analysed food baskets (Ericson et al., 2008; Kärrman et al., 2009; Haug et al., 2010; Vestergren et al., 2012), or employed food consumption questionnaires (Halldorsson et al., 2008; Rylander et al., 2010) to link diet with plasma or serum concentrations. The results are not consistent, which suggests multiple sources and ubiquitous distribution of these compounds. Study cohort characteristics (e.g., age, gender, socioeconomic factors and life-style issues, and the year of sampling) likely have influenced the results. Until recently, PFOS was thought to be fairly uniformly distributed in food items. However, dietary items consumed by indigenous populations in Arctic regions, such as fish and marine mammals, appear to be major predictors of exposure by analogy to the legacy POPs (Dallaire et al., 2009; Ostertag et al., 2009).

The PFAS concentrations in whole blood, plasma or serum have varied. The highest concentrations have been observed in populations of industrialized northern hemisphere countries (Kannan et al., 2004), although PFAS concentrations for Australian adults have shown to be of comparable magnitude (Kärrman et al., 2007a). The ability for PFASs to cross the placenta have been shown in several studies (e.g., Inoue et al, 2004; Midasch et al., 2006; Fei et al., 2007; Monroy et al., 2008). In general, the concentrations reported have been the half of the maternal concentration. After delivery, the new-born child continues to be exposed to PFASs through breast milk. Even though PFOS concentrations in breast milk are typically 1% of the corresponding maternal serum concentration, corresponding value for

PFOA is 12% (Kärrman et al., 2007b), the amount milk consumed still makes this exposure pathway significant.

After the phase-out of the ECF production (see Figure 3), PFAS concentrations in the general population have decreased. Analysis of pooled serum samples from Norwegian men collected from 1976 to 2007 revealed declining concentrations of perfluorohexane sulfonic acid (PFHxS), PFOS and PFOA, but not for longer chain PFCAs (Haug et al., 2009). A similar trend was observed for serum samples from Red Cross blood donors in the U.S sampled in the period 2000-2010 (Olsen et al., 2012). However, the continued PFOS production in China (Butt et al., 2010) might affect time trends for other geographical areas.

1.4.3 cVMS

Compared to PFASs, POPs and other environmental contaminants, fewer HBM studies have focused on cVMS. In a recently published study, siloxane concentrations in plasma from a population working and living near a siloxane production facility was reported (Xu et al., 2012). Other published reports on cVMS in humans have investigated amounts in adipose tissue (US EPA, 1987), whole blood and plasma collected from women with silicone breast implants (Flassbeck et al., 2001). Flassbeck et al. (2003) also reported cVMS in fat and muscle tissues from women with breast implants. One or more of D4, D5 and D6 have been found in 11 out of 49 samples of human breast milk in an environmental siloxane survey by the Swedish EPA (Kaj et al., 2005b). The need for more knowledge about cVMS exposure from PCPs has recently been highlighted by several authors (Horii and Kannan, 2008; Wang et al., 2009).

Environmental human exposure to cVMS is not considered to be of great concern (Brooke et al., 2009a-c). However, it is evident from the studies by Horii and Kannan (2008) and Wang et al. (2009a) that humans by usage of cosmetics and PCPs can become exposed because of the high concentrations of cVMS in some of these products. The content of cVMS in PCPs varies widely, from a few percent to more than 90 percent (Brooke et al., 2009a). The content and composition of cVMS in a wide range of PCPs have been reported for Canada, United States, Japan and China (Horii and Kannan, 2008; Wang et al., 2009; Lu et al., 2011); D5 was the dominant siloxane in PCPs, except in China where linear siloxanes were most prevalent). Based on daily PCPs usage and mean concentrations, the daily exposure to total siloxanes (linear and cyclic) was estimated to 307 mg/day for women in the United States (Horii and

Kannan, 2008). The corresponding values for Canadian and Chinese women were 996 mg/day and 4.51 mg/day, respectively (Wang et al., 2009; Lu et al., 2011). The high volatility of cVMS implies that air is a potential exposure pathway, although the primary route for humans can be presumed to be dermal absorption following application of PCPs. Of course, exposure through inhalation would be pertinent in occupational settings (Cornelis, 2005). The concentrations of cVMS in dust appear to be low, with a calculated daily exposure to total siloxanes from this source of 15.9 ng/day in China (Lu et al., 2010).

1.5 Health Effects

1.5.1 PFASs

Due to the widespread distribution and persistence of these compounds, several research groups have elucidated their toxicity and toxicokinetics. Since PFOS and PFOA are the most common PFAS in biological matrices, the majority of such studies have investigated these end products.

PFAS are readily absorbed in the gastrointestinal tract (Lau et al., 2004). They are distributed into the extracellular volume (Noker and Gorman, 2003; Butenhoff et al., 2004), and is also found in liver, kidney and blood (Lau et al., 2007). Ionic PFAS are associated with β-lipoproteins, liver fatty-acid binding proteins and albumin (Luebker et al., 2002; Han et al., 2003; Jones et al., 2003). They are not known to be metabolised, and are excreted by way of urine and bile. Elimination rates differ considerable between species, and for some species also between sexes (Lau et al., 2007). Humans eliminate PFASs very slowly compared to other species and could be explained by renal reabsorption and enterohepatic circulation (Harada et al., 2005; 2007). In retired fluorochemical production workers, the geometric means of half-lives were: 4.8 y (PFOS), 3.5 y (PFOA), and 7.3 y (PFHxS) (Olsen et al., 2007a). The half-lives of PFOA and PFOS have recently been confirmed to be within the same range (Seals et al., 2011; Olsen et al., 2012).

The liver is considered to be the primary target organ with respect to exposures from PFOS and PFOA (Cui et al., 2010). Repeat-dose studies of both compounds in rodents have reported reduced body weight, increased liver weight, and reduced cholesterol levels (Lau

et al., 2007). Other toxicological findings in addition to liver toxicity for PFOS and PFOA are neurotoxicity and immunotoxicity (Dewitt et al., 2012; Viberg and Eriksson, 2011). Both PFOS and PFOA affect peroxisome proliferator activated receptors (PPARs), which constitute a group of nuclear receptor proteins that function as transcription factors and thus regulate gene expression (Viberg and Eriksson, 2011).

The majority of developmental toxicology studies involved *in utero* exposure of PFOS and PFOA in rodents. Exposure to these compounds during the gestational period has caused toxic effects in both the foetuses and new-born pups. For high exposures, birth defects have been seen in both rats and mice (Thibodeaux et al., 2003), as well as reduced postnatal survival of their neonates and delays in growth and development in the surviving pups (Lau et al., 2004). Gestational exposure to PFOS can alter the thyroid hormone system in both rats and mice during development, and can be one of the mechanisms of action behind the developmental toxicity of PFOS (Viberg and Ericsson, 2011).

Several epidemiological studies have been conducted to evaluate the impact on humans. In occupational studies, the outcome of PFAS exposures have been inconsistent, and no clear causal effect has been established. Steenland et al. (2010) conclude that the data are insufficient to draw firm conclusions about adverse health outcomes. By contrast in a large population-based study (The C8 Health Project, Little Hocking, Ohio, USA; Frisbee et al, 2009), of a population exposed to high concentrations, significant positive associations were observed in children and adolescents between serum concentrations of PFOA and PFOS and total serum cholesterol, low-density lipoprotein cholesterol and thyroxine (total T4). A significant reduction in calculated thyroid hormone (T3) uptake was also observed (Knox et al., 2011). It should be noted that these exposures were atypical and thus their relevance to more normal exposure is not clear. In the US National Health and Nutritional Examination Survey (NHANES), elevated serum concentrations of PFASs were associated with chronic kidney disease ($p<0.0001$) (Shankar et al., 2011). Interestingly, a study conducted in the Faroe Islands reported an association between PFAS serum concentrations and lower antibody responses to childhood immunization. Reduced antibody concentrations can impair long-term protection (Grandjean et al., 2012).

Due to the developmental toxicology reported in animal studies of PFASs, there has been a focus on human developmental outcomes such as birth weight and length, and head circumference (Olsen et al., 2009). The overall picture that has emerged suggests that PFASs exposure is not associated with any clinical relevant birth outcomes, in spite of a recently

reported negative correlation between maternal PFOS concentrations and fetal plasma T3 levels ($r=-0.41$, $p<0.05$ after adjustment; Kim et al., 2011a)

One of the challenges in interpreting these studies concerns differences in half-lives of these chemicals in humans, and as observed in animal research models. For the latter, the exposure doses used were generally considerably higher than what has been reported for the general human population. Information about long-term chronic exposure to low doses or of combined effects would better reflect the real exposure experienced by wildlife and humans, however this information is scarce.

1.5.2 cVMS

The majority of reports that investigate the absorption, excretion and toxicity of D4 and D5 have involved experimental animals. Based on this, the amount of cVMS absorbed differs between the three uptake routes: inhalation, dermal contact and oral ingestion. In animals, around 5% of inhaled D4 and 3% of D5 is absorbed; the corresponding value for D4 in humans is 6-17%. When administered to animals in corn oil, 52% (D4) and 20% (D5) are absorbed (Brooke et al., 2009a,b). In both rats and humans, dermal uptake is relatively low for D4 [<1% (rat) and 0.5% (human) of the applied dose]; for D5 the corresponding human value is 0.04% (Jovanovic et al., 2008). Based on the D4 and D5 data, the inhalation absorption for D6 is estimated as 3 %. The oral bioavailability of the latter appears moderate (15%), and its dermal absorption is expected to be around 0.1% (Brooke et al., 2009c).

As mentioned in Section 1.2.2, most of cVMS applied to the skin (90%) volatilize rapidly due to their high volatility (Reddy et al., 2007; Jovanovic et al., 2008). Thus inhalation after evaporation from the skin could be an exposure source (although suspected to be minimally so). Absorbed cVMS distribute widely in the body (Kala et al, 1998). The cVMS are highly lipophilic, with considerable fat-to-blood partition coefficients (in rats;~2000 and 500 for D5 and D4, respectively and likely similar in humans), leading to storage in lipid tissues (Plotzke et al., 2000; Andersen et al., 2001; Tobin et al., 2008). After inhalation or dermal exposures of D4 and D5, cVMS are eliminated through respiration (Andersen et al., 2001; Tobin et al., 2008), or by way of metabolic degradation (excretion by urine) (Varaprath et al., 2003). Urinary excretion as water-soluble metabolites (silanols) and exhalation of the parent compounds are the main elimination routes and forms in experimental animals, with loss by faeces being minor (Brooke et al., 2009a,b). Unlike D4 and D5, most of D6 is eliminated

unchanged in exhaled air. No parent compounds could be detected in urine when the metabolic transformation of D5 and the linear siloxane hexamethyldisiloxane was investigated (Varaprath et al., 2003). Transformation products for both these two compounds and also D4 (Varaprath et al., 1999) included the common metabolite $Me_2Si(OH)_2$ (among other products), which reduces the suitability of urine for the determination of cVMS. The half-life of D5 in male and female rats depended on dose, gender, and number of repeated exposures and differed between tissues. The following half-lives ($t_{1/2}$) for a single 6-h exposure of females were typical: 50 h (plasma), 80 h (liver and lung), and 495 h in fat; $t_{1/2}$ values for males were mostly longer (Tobin et al., 2008). Population half-lives have recently been reported for retired workers in a manufacturing plant in China (Xu et al., 2012); they increased with increasing number of Si-O bonds and ranged from 2.34 (D4) to 3.15 (D6).

The mammalian toxicology of D4, D5 and D6 has been summarized by Brooke et al. (2009a-c). Most of the studies have been conducted for D4. Exposures to D4 by oral or inhalation administration caused several biological responses in rats, such as estrogen mimicry (McKim et al., 2001**)** and liver enlargement. As a consequence, D4 has been replaced in many formulations by D5 (Reddy et al., 2008; Brooke et al., 2009a), even though liver enlargement has also been observed for D5. There is some evidence that D4 (but not D5) could lead to impaired fertility in rats, although the suggested reproductive mode of action involved would likely not be relevant for humans (Siddiqui et al., 2007a,b). Specific fetal developmental effects were not observed. The no observed adverse effect level (NOAEL) estimate for fertility effects based on rat studies for D4 (105 mg/kg/day; also assigned to D5) was considerably higher than that at which a toxicologically significant liver enlargement was seen for both (NOAEL of 19 mg/kg/day) (Brooke et al., 2009a,b). Thus the latter outcome is likely the primary systemic health effect relevant for humans. Compared to D4 and D5, the magnitude of liver enlargement due to D6 was relatively small. Overall, no toxicological hazards have been identified for D6 (Brooke et al., 2009c).

2. STUDY OBJECTIVES

The work described had two primary objectives. 1. Assess maternal and new-born exposure to perfluoroalkyl substances in regions for which this information was lacking (no or limited data), namely South Africa, Uzbekistan and arctic Russia. 2. Quantify cyclic methylsiloxanes in blood plasma of pregnant and postmenopausal women.

More specifically the subgoals were to assess:

- Geographical differences in PFAS exposures in South Africa (rural *versus* urban site comparison of maternal serum and cord blood concentrations) (Paper I);
- Distribution of PFAS between whole blood and plasma from Uzbekistani and Russian delivering women and their new-borns (cord blood) (Paper II);
- Relative abundance of isomers of PFOS and FOSA (Paper II);
- Determine cVMS plasma concentrations in pregnant and postmenopausal women selected from the general population in relation to self-reported use of PCPs (Paper III).

3. MATERIALS AND METHODS

3.1 STUDY POPULATIONS AND SAMPLING DETAILS

This thesis was based on samples from study populations in four different countries.

3.1.1 The South African study (Paper I)

The South Africa study group consisted of 71 delivering women and their new-borns, of whom 58 also provided a cord-blood sample. Participating women were recruited from those who presented for delivery at provincial delivering hospitals, and represented six different South African communities. The locations included (see Figure 5): the city of Johannesburg; industrial communities dominated by coal mining, stainless steel production, fishing, and gold mining; and malaria endemic communities (one coastal and one inland). In addition all women answered a socioeconomic questionnaire (see Appendix 1). The majority of the participants were of African Black ethnicity and were of comparable economic status. Maternal age ranged from 14-41 y (mean: 25 y). Blood samples were collected in the period November 2005 to December 2006.

Figure 5. Geographical locations of study sites in South Africa: Site 2 = urban (Johannesburg); Site 3 = industrial; Site 4 = Atlantic Ocean; Site 5 = mining; Site 6 = coastal malaria area; Site 7 = inland malaria area.

3.1.2 The Russian and Uzbekistan study (Paper II)

Sampling of human blood was undertaken in parallel with the dietary and lifestyle surveys of the GEF/UNEP/AMAP/RAIPON project "Persistent Toxic Substances (PTS), Food Security and Indigenous Peoples of the Russian North" (AMAP, 2004b). The sampling period in the Russian Arctic (city of Norilsk) was from October to December 2001, and April to June 2002 in the Aral region of Uzbekistan (see Figure 6 for map). All delivering women were invited to participate when in the hospital delivery departments. Mothers from Norilsk city (Taimyr okrug of Krasnoyarsk kraj; n=7) were non-indigenous. Mothers from Urgench (n=6) and Khazarasp cities (n=4) (Khorezm oblast, Uzbekistan, about 200 km from the Aral Sea) were indigenous Uzbeks. The maternal median age at delivery was 24 (range 24-28) and 25 (range 21-41), respectively for the Norilsk and Uzbekistan study groups. Of the Uzbekistan mothers 60% had 2-8 children, while 71% of the Norilsk mothers had one child and 29% had two (means of 2.7 and 1.3 respectively). Blood was collected from mothers during the first three

days after delivery. Cord blood was sampled immediately after tying and cutting off the umbilical cord. For whole-blood sampling, Becton Dickinson Vacutainer System (USA) with K_2-EDTA was used (BD 366457). An aliquot of whole blood was centrifuged at 3 000 rpm to separate blood cells from plasma. Cord blood was treated in the same manner.

Figure 6. Map of the Russian Arctic and Uzbekistan with the regions involved in this study highlighted (AMAP, 2004b).

3.1.3 The NOWAC and MISA cohorts (Paper III)

The Norwegian Women and Cancer study (NOWAC) is a prospective cohort study, which consists of more than 172 000 women who answered detailed questionnaires regarding their diet and lifestyle (Lund et al., 2008). From the original cohort, 50 000 women (born between 1943 and 1957) were recruited randomly to the NOWAC postgenome study (Dumeaux et al., 2008). The women also donated blood samples (blood was drawn in 2005 into Greiner Bio-One sodium citrate coagulation tubes), and from a randomly selected batch of 500, 332 plasma samples were analysed with respect to paraben content (Sandanger et al., 2011). From this batch of 332 women, 94 samples were randomly selected and analysed

with respect to cVMS contents. The participating women were 48 to 62 years old, and thus may be designated postmenopausal. The NOWAC participants were drawn from a cohort for whom the external validity has been confirmed, and thus the women were representative of the Norwegian women at their age (Lund et al., 2003). Information on use of PCPs was ascertained from a questionnaire that was self-administered just before enrolment and prior to the blood sampling (for details see Sandanger et al., 2011 and Lund et al., 2008), and thus does not specifically apply to the day of sampling. The questionnaire also sought information about breast implants.

The North Norwegian Mother-and-child Study [also referred to as the MISA Study (Miljøgifter i svangerskapet og ammeperioden)] is a longitudinal cohort study which consists of 515 women who have answered detailed questionnaires regarding their diet and lifestyle. Pregnant women in the study area were invited by written invitation administrated by ultrasound clinics personnel or during midwife consultations (Hansen et al., 2010). From June 2007 to March 2009, 2600 women were invited, 609 responded, 557 were registered, 542 gave a blood sample, and 27 were excluded because of the lack of written consent. Thus, 515 women initially were included in the study. Serum samples were collected in BD Vacutainers (SST II Plus Advance 10/8.5 ml), however testing of extracts from various sample collection tubes revealed the presence of high concentrations of cVMS in these specific vacutainers. At the end of the recruitment period, it was possible to collect a small number (n = 17) of plasma samples and red blood cell (RBC) fractions for cVMS analysis using BD Vacutainers (K2E 10.8 mg, 6.0 mL) tubes. The sampling period was between February and May 2009, during week 11 to week 23 of pregnancy.

3.2.1 Analysis of PFAS

The analytical details are provided in Papers I and II, and only a brief overview is provided here. The plasma/serum and whole blood extraction and clean-up methods for the PFASs were similar in Papers I and II, and involved modifying the methods described by Powley et al. (2005). In short, internal standards were added to plasma, serum or whole blood, and the sample was extracted with methanol. The extract was cleaned up with acidified EnviCarb. Before analysis recovery standard was added. In Paper I, the sample components were separated by HPLC and quantified by mass spectrometry (QToF, Waters), while the Paper II analyses were achieved by ultra high pressure liquid chromatography triple-quadrupole mass-spectrometry (UHPLC-MS/MS, Thermo Scientific). In Paper I, only two ^{13}C labelled internal standards (PFOS and PFOA) were used for quantification. In the Paper II work, multiple ^{13}C- labelled internal standards were used (specifically; PFOS, perfluorooctane sulfonamide (FOSA), perfluorobutanoic acid (PFBA), perfluorohexanoic acid (PFHxA), PFOA, perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnDA), and perfluorododecanoic acid (PFDoDA)) and ^{18}O for PFHxS.

3.2.2 Analysis of cVMS

To a known amount of plasma or RBC fraction, mass-labelled internal standards were added together with 1 mL of hexane. After shaking and centrifugation, a recovery standard was added to a known aliquot. Subsequently, the chromatographic analyses of the NOWAC samples were performed on a HP 6890 series gas chromatograph, and the isomer identification was done on a HP 5973 mass selective detector (Agilent). The chromatographic analysis of the MISA samples was achieved with an Agilent 5890N gas chromatograph, and the isomer identification was conducted by high-resolution mass spectrometry on a Waters Autospec-V Ultima in positive electron ionization mode (EI+, 35 eV). Additional details are provided in Paper III.

3.3 Statistical Analysis

Statistical analyses were carried out using the Data Analysis and Statistical Software (STATA) package versions 10.0 (Paper I) and 12.0 (Papers II). In the Paper III data analysis, the Statistical Analysis System (SAS) version 9.0 was used. Details of the statistical approaches are described in the respective papers together with the different approaches used for calculating limit of detection (LOD), limit of quantification (LOQ) and method detection limit (MDL). Due to the non-normal distribution of the contaminant concentrations, log-transformed values (base 10) were used in the statistical analyses in Paper I. To assess differences between study sites and cohorts, non-parametric tests were used in Paper II.

3.4 Ethical Considerations

Paper I

An ethics clearance certificate (Protocol Number M040314) was granted for the study by the Committee for Research on Human Subjects of the University of the Witwatersrand, Johannesburg, South Africa. In addition, informed written consent was obtained from each participant prior to inclusion in the study.

Paper II

The study protocol, training of personnel and the sample collection strategy concurred according to those adopted by the AMAP Human Health Assessment Group (AMAP, 1998). The study protocol was also approved by the Ethical Committee at the Pasteur Institute, St Petersburg (international reference # T5096). Written informed consent was obtained from the participating delivering women.

Paper III

The NOWAC cohort secured approval from The Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate for the basic collection and storing of questionnaire information, blood samples and tumour tissue from present. All women completed an informed consent for later linkages to the Cancer Registry of Norway, the Norwegian Mammographic Screening Programme, and the register of death certificates by

Statistics Norway (Dumeaux et al., 2008; Lund et al., 2008). Each sub-project within the NOWAC cohort has received approval from the Regional Committee for Medical Research Ethics.

The MISA study was also approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate. Participation was voluntary, and the women signed an informed consent form.

4. Results – Summary of Papers

4.1 Paper I

Perfluorinated compounds in maternal serum and cord blood from selected areas of South Africa: results of a pilot study

Because the information about PFAS concentrations in humans in the southern hemisphere was sparse, this study was designed to assess them in serum from delivering women and cord blood from selected areas of South Africa. The majority of the participants were of African Black ethnicity with a similar economic status. The reported PFAS concentrations were low, where PFOS was the most abundant compound (median of 1.6 ng/mL, with a range <0.1 - 15.9 ng/mL and LOD = 0.1 ng/mL) followed by PFOA (median of 1.3 ng/mL, range 0.17-8.5 ng/mL). Concentrations in umbilical cord samples were similar to maternal serum. Linear PFOS in maternal samples accounted for 58% of total PFOS, and this was comparable to that reported for Australian women (59%) but lower than reported in a Vietnamese study (83%). There were significant differences ($p \leq 0.05$) in maternal PFOS concentrations between the communities, with the highest concentrations observed in urban and semi-urban areas. The data suggest different exposure patterns for these compounds compared to other countries.

4.2 Paper II

Partition of perfluoroalkyl substances (PFAS) in whole blood and plasma, assessed in maternal and umbilical cord samples from inhabitants of arctic Russia and Uzbekistan

The Norilsk mothers (living in the Russian Arctic) had significantly higher plasma PFOS concentrations, with a median of 11.0 ng/mL (range 5.56-14.5 ng/mL) compared to 0.23 ng/mL (range < 0.08 - 0.89 and MDL = 0.08) for the Uzbekistani women; PFOS was the only PFAS present in more than 80% of the samples for the latter group.

Partition between the different compartments of blood was investigated for the Norilsk samples only. The plasma-to-whole blood ratio for ionic PFASs in delivering women were somewhat lower (≈1.6) than reported elsewhere for adults (>2). The corresponding ratios for umbilical cord samples were somewhat higher. In both instances, the observed ratios were

similar to those calculated *a priori* from known blood plasma and cell volumes. FOSA had a different distribution that reflected its acid-base properties, with the major amount residing in the blood cell fraction. For both carboxylate and sulfonate PFASs, increasing carbon chain length correlated with higher maternal-cord ratios for both whole blood and plasma. This suggests decreased placental transfer. The median percentages of linear PFOS in plasma and whole blood were comparable (50.5 and 46.6, respectively) and lower than reported for the manufactured technical mixture (≈70%). A semi-quantitative determination for FOSA yielded even lower values (44.6% in plasma and 40.8% in whole blood). The observation that a large fraction of FOSA is associated with the cell fraction implies that the body burden of this compound has been underestimated because until now plasma (or serum) was the body fluid mainly monitored. This has led to an underestimation of exposure.

4.3 PAPER III

Plasma concentration of cyclic volatile methylsiloxanes (cVMS) in pregnant and postmenopausal Norwegian women and self-reported use of personal care products (PCPs)

The wide use of silicones and the ubiquitous presence of cVMS in laboratory air makes their analysis challenging. Several procedures were implemented to avoid inadverted contamination of the samples.

For the NOWAC samples, more than 85% of the women had D4 concentrations above the LOQ (2.74 ng/mL), while the detection frequency was only 18% for the MISA participants. The highest cVMS concentrations were observed for the NOWAC middle-aged women. In both cohorts, D4 was the most prominent compound with maximum plasma concentrations of 12.7 ng/mL (NOWAC) and 2.92 ng/mL (MISA). The other investigated cVMS, namely D5 and D6, were below the detection limit in most of the samples. There were no significant correlations between the concentration of D4 and the reported total body cream use, however the median increased with increasing percentage of body creams. Sampling period (2005 *versus* 2009) and/or age of the women could explain the differences between the two cohorts.

5. DISCUSSION

5.1 HUMAN BIOMONITORING OF PFASS

5.1.1 Observed concentrations in perspective

The reported PFAS concentrations in Paper I and II show large variations and predictors that may explain these differences are discussed below.

Emission history and its effect on place of residency and time of sampling (including birth year of the mother) seems to be a relevant predictor for maternal PFOS concentration (implied by Figures 3 and 7). The observed PFOS (sum of branched and linear) and PFOA concentrations for arctic Russia, Uzbekistan and South Africa have also been compared to reports from other countries. The maternal sample concentrations in these figures represent the exposure at the end of pregnancy or at delivery, except for Beesoon et al. (2011) for which the samples were from gestational week 15. Other than the South African data, the concentrations depicted in Figures 7 and 8 are for Northern Hemisphere countries. With respect to PFAS emissions, the developed countries are more affected; this is reflected in the higher concentrations compared to undeveloped countries (Lau et al., 2007; Martin et al., 2010). Clearly geographical localisation and living standard are strong predictors, and hence Uzbekistan and South Africa are less impacted compared to developed countries. The PFAS concentrations also reflect the year(s) of sampling, however interpretation of the time trends in Figure 7 must been done with care. It seems that the PFOS concentrations in delivering women residing in countries in the northern hemisphere have decreased over time. This is in agreement with that observed for general population study groups in the USA and Norway (see Section 1.4.2), as well as the reduction in production (see Figure 3). Consequently, the year of sampling should have an impact on the concentration magnitude observed. This trend is less prominent for PFOA, since its production continues by the telomerization manufacturing process (Benskin et al., 2010). Also, PFOA seems to be more ubiquitously distributed (Vestergren and Cousins, 2009). This is supported by our observation that South Africa concentrations were of comparable magnitude with values from Northern hemisphere countries (see Figure 8). The low bioaccumulation potential of PFOA relative to PFOS (Conder et al., 2008) presumably contributes to the narrow concentration ranges.

In the South African study we investigated the association between maternal age and PFAS concentration, and found no significant relationship. Dependence on age (and also sex) has been observed in some studies (Ericson et al., 2007; Hölzer et al., 2008), but not in others (Calafat et al., 2007; Midasch et al., 2006). For legacy POPs like PCBs, recent modelling has emphasized the importance of considering birth year and sampling year in relation to emission history (Quinn et al., 2011). In a cross-sectional study it is important to evaluate the PFAS concentrations in relation to age structure of the cohort/maternal age, year of sampling and historic emissions.

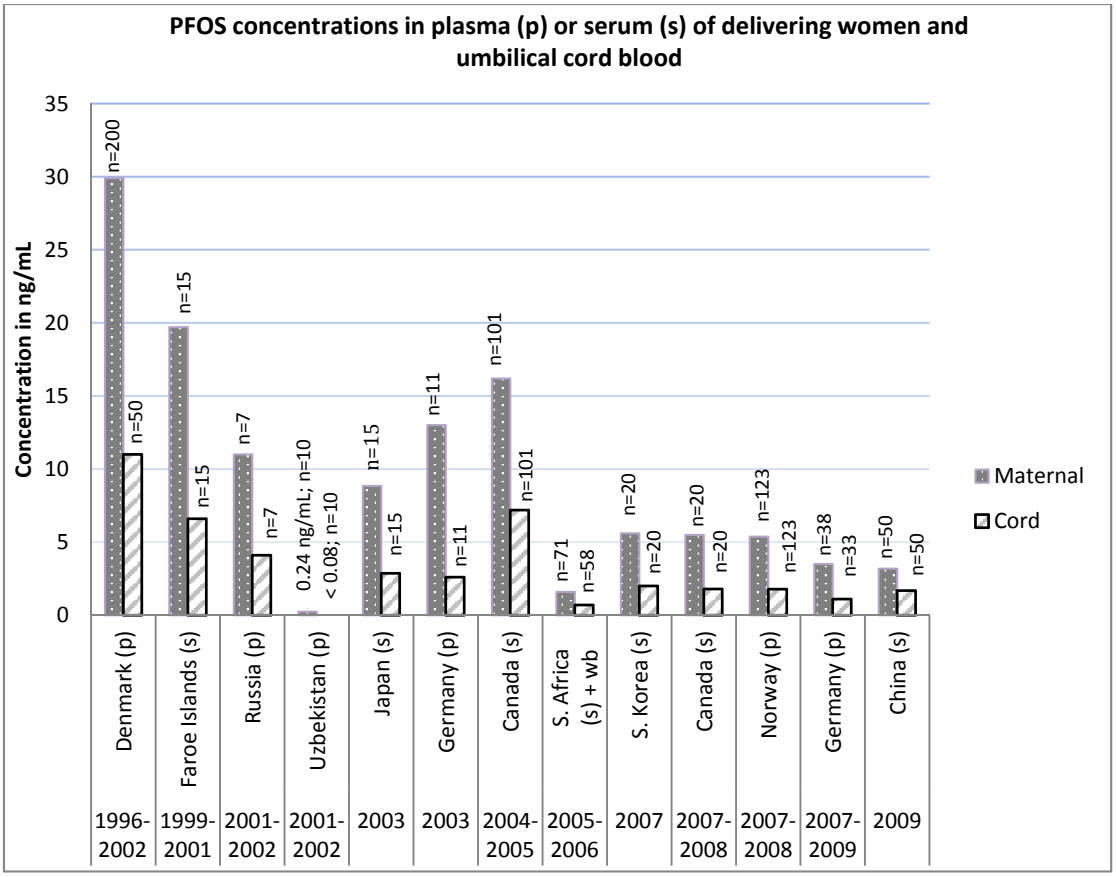


Figure 7. PFOS concentrations in plasma (p) or serum (s) of delivering women and umbilical cord blood (UCB). All studies had the same matrices for maternal and UCB samples, except for South-Africa where maternal serum and UCB whole blood (multiplied with a factor of 2) were compared. For Russia, Uzbekistan and South Africa sum-PFOS (i.e., liear and branched) is reported. The figure is based on the following publications: Denmark, Fei et al., 2007; Faroe Island, Needham et al., 2011; Russia, Hanssen et al., 2013; Uzbekistan, Hanssen et al., 2013; Japan, Inoue et al., 2004; Germany, Midasch et al., 2007; Canada, Monroy et al., 2008; South Africa, Hanssen et al., 2010, South Korea, Kim et al., 2011b, Canada, Beesoon et al., 2011, Norway, Gützkow et al., 2011; Germany, Fromme et al.,2010 ; China, Liu et al., 2011.

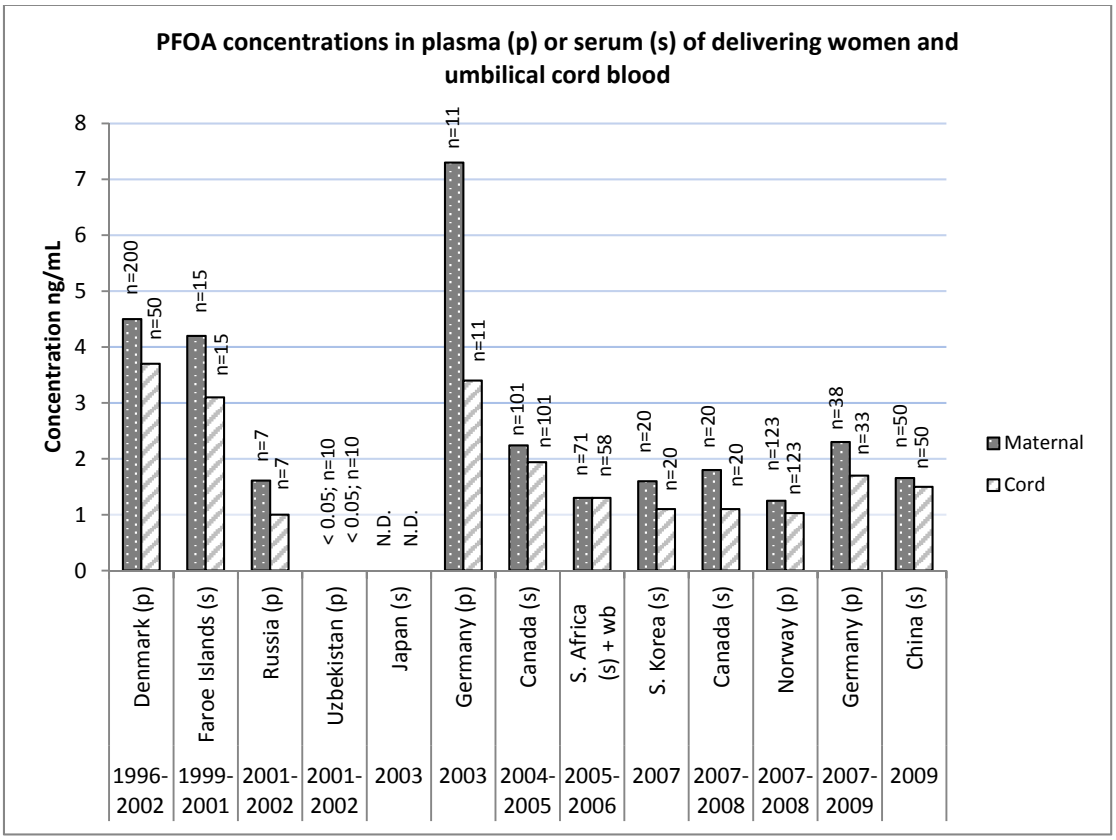


Figure 8. PFOA concentrations in plasma (p) or serum (s) of delivering women, and in umbilical cord blood (UCB). All studies had the same matrices for maternal and UCB samples, except for South-Africa where maternal serum and UCB whole blood (multiplied with a factor of 2) were compared. N.D, not detected. See legend to Figure 8 for list of publications consulted.

Higher PFAS concentrations in samples from Norilsk compared to Uzbekistan indicate a difference in exposure. To help in the interpretation of this finding, a brief discussion ensues about identified sources for legacy POPs in the study communities. From the AMAP report (2004b), we know that the delivering women in Norilsk (both indigenous and non-indigenous) had elevated PCB concentrations, while they were considerably lower for the Uzbekistani group. By contrast, the pesticide derivative *p,p'*-DDE was considerably higher for the latter subjects. This suggests differences in exposure scenarios. The Uzbekistani women were known to be exposed to pesticides from local use and this was reflected especially in their plasma concentrations of *p,p'*-DDE (Sandanger et al., 2009). It is well known that Arctic populations are affected by LRT and that traditional foods such as fish are consumed as well as marine mammals by subpopulations. These are known sources of PCBs and

organochlorine pesticides due to their bioaccumulation and biomagnification in these species (AMAP 1998, 2003, 2004a,b; Ostertag et al., 2009).

As illustrated by the plasma concentrations depicted in Figure 9, PFAS are known to be present in the Arctic and , in addition to local sources, LRT is suspected (see Section 1.3.1). The presence of PFOS and PFOA in blood samples from Norilsk with concentrations of comparable magnitude to those reported for Northern Hemisphere industrialised countries (see Figures 7 and 8), support this interpretation. The seven women investigated in Norilsk were non-indigenous and mostly consumed store bought foods (primarily non-local). Plant cultivation in Norilsk area was minimal. Because of regional reindeer breeding, fishing and hunting activities, there was some consumption of tundra reindeer, ptarmigan, and fish. The Uzbekistani women had a diet that featured a variety of items produced locally (e.g., meat, poultry, fish, cereal, fruits and vegetables), and the reported PFAS concentrations for these women were low (see Figures 8 and 9; most of the samples had PFOA concentrations below the MDL). There is no information available on the content of PFAS in food and food packaging from Russia and Uzbekistan. It is suspected that it was low in prior to and during the sampling period (personal communication, A.A.Dudarev). Diet has been suggested as the major source and thus a likely predictor for PFAS concentrations in body fluids (Vestergren et al., 2012), and might thus serve as a reflection of the emission history. Since the phase-out of POSF production, diet as a direct exposure source will become a more prominent predictor compared to more indirect sources such as dust and indoor air. The latter are and will be influenced by the phase-out of PFASs from consumer products.

Although environmental measurements for both these areas are scarce and as already mentioned, it is likely that the Norilsk area is affected somewhat by its industrialization in addition to LRT. One report on PFASs in snow from arctic Russia confirms the latter (Saez et al., 2008). A delay in LRT might be a possibility and, if so, the concentrations in the Arctic environment might even increase after the phase out (Armitage et al., 2009). Consequently, the concentrations of PFAS in the diets of residents of the Arctic might thus rise for some time based on this scenario (i.e., emission history is important). The low maternal plasma concentrations observed confirm that the environment in Uzbekistan is not contaminated with PFAS.

The PFASs emission in the Southern hemisphere is limited (Hanssen et al., 2010, Paper III). In the South Africa population studied, the PFOS concentrations were low, while those of PFOA were comparable to Norilsk (Figures 7 and 8). For the South-Africa study groups, the

observed concentrations of PFOS and PFOA were significantly higher in semi urban/urban *versus* rural areas. Differences in diet, housing and use of consumer products were important predictors of the reported concentrations.

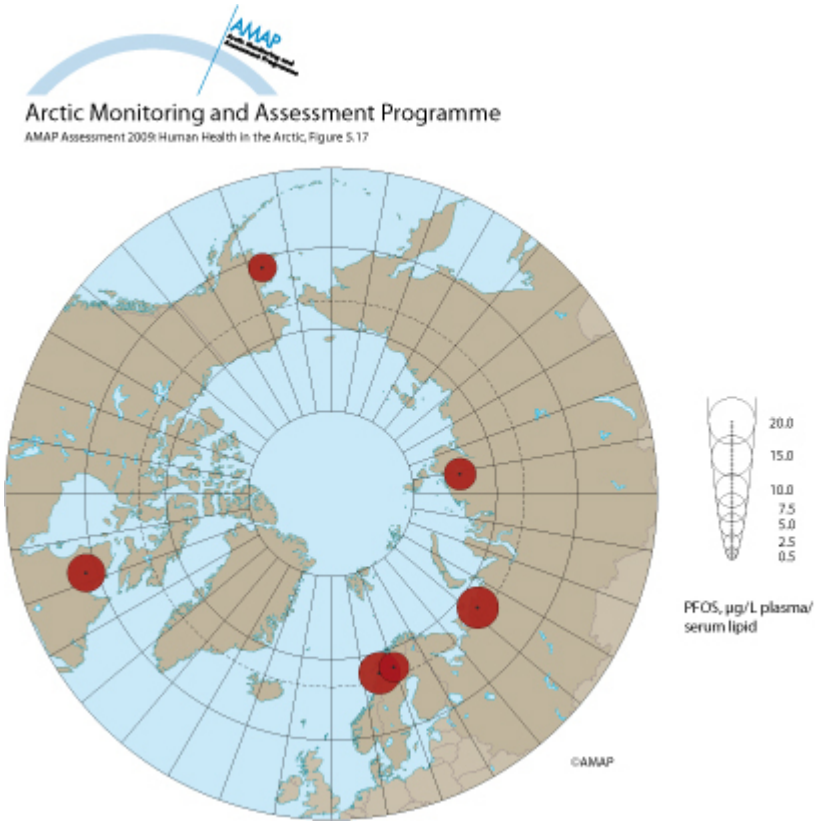


Figure 9. PFOS concentrations (µg/L) in plasma of mothers, pregnant women and women of child-bearing age in the circumpolar countries (AMAP, 2009, revised 2012). The wording "serum lipid" in the figure does not apply.

It was not possible to evaluate breastfeeding as a predictor for maternal PFAS concentrations due to the quality of this information in our studies. Even though the PFASs concentration in breast milk are considerably lower than maternal serum, the transfer to the child by breast milk is still considered significant (Kärrman et al., 2007b). This suggest that the number of children (see placental transfer below) and breastfeeding would affect the maternal PFAS concentration in blood.

The PFASs in human blood samples most frequently reported in recent publications besides PFOA and PFOA are PFHxS and long chain PFCAs such as PFNA, PFDcA and PFUnDA. Ideally,

the presence of PFNA and PFUnDA in the Norilsk samples could indicate an exposure source from an ECF production, since telomerisation yield only even numbered carbon chains. However breakdown products of telomers, such as 8:2 FTOH and 10:2 FTOH, could also yield these compounds (Ellis et al., 2004; Sinclair and Kannan, 2006). Even though the concentrations of PFASs other than PFOS and PFOA are considerably lower, it is of importance to continue monitoring them. Rationale for this includes the observation by Haug et al. (2009) and Glynn et al. (2012) that the decline in concentration of 'other' PFASs of the POSF production was not as rapid after the phase-out. Concern remains about continued human exposure, especially now that PFOS production in China is suspected (see Section 1.4.2). The production volumes (<300 tonnes per year) in China are lower than those previously reported for 3M (see Figure 3) (Lim et al., 2011), however the impact on the environment of neighbouring countries like Uzbekistan and Russia cannot be disregarded.

In conclusion, many of the exposure source factors and body-fluid contaminant concentration predictors discussed in Section 1.4.2 for PFASs appear to be reflected in the country differences observed in the present study.

5.1.2 Blood matrices

As mentioned in Section 1.4.2, serum (or plasma) has been the matrix of choice for biomonitoring of PFASs. Whole blood is considered a difficult matrix and is not routinely used in clinical chemistry measurements (Ehresman et al., 2007). Using serum or plasma for legacy POPs analysis has been appropriate since these compounds are associated with the lipid fraction. The ability PFASs have to bind to albumin also suggests that serum or plasma is the appropriate matrix for these compounds. However, the question to ask is: do we get the complete picture of exposure analysing only serum or plasma? D'Eon and Mabury (2010) reported that in paired whole blood and plasma samples from rats, the concentration of mono-perfluorinated phosphonic acids (mono-PFPA) was equal in plasma and whole blood. This suggested that this compound may associate with blood cells, leading to an underestimation of their concentration in serum and plasma. Using appropriate packed cell and plasma volumes for neonates and pregnant women at term, plasma-to-whole blood dilution factors were calculated in the current project. These values were 1.6 (maternal) and 2.5 (umbilical cord), and were in good agreement with those observed for PFOA, PFNA, PFHxS and PFOS (see Figure 10). The observed ratio for PFUnDA was somewhat lower than

predicted in both instances [medians of 1.44 (maternal) and 1.86 (cord)], which might have been biased by its low detection frequency. Indeed plasma or serum seems to be a suitable matrix for the majority of ionic PFASs, and thus nothing seems to be lost when the cell fraction is removed.

For FOSA the ratios were distinctly different [medians of 0.14 (maternal) and 0.78 (cord)] (see Figure 10). Using the pK_a of 6.27 for FOSA and the pH of blood as 7.37, calculations showed that approximately 7% of the compound would be uncharged or in a neutral form, and this estimate is close to what we observed in the plasma fraction. This implies that most of the FOSA resides in the blood cell fraction as the sulfonamidate ion, which concurs with the maternal whole blood/plasma concentration ratio observed of 7.14 (i.e., 1/0.14). This preference for whole blood is also reflected in the cord whole blood/plasma concentration ratio, but less dramatically so (see also 5.1.3). It has been pointed out that the negative charge of this ion is stabilized by resonance and is thereby reduced [i.e., its negative point charge is spread over the nitrogen and oxygen atoms of the sulfonamidate moiety, ($–SO_2–NH_2$)]. Additional details are provided in Paper II.

Since most of FOSA occurs in the cellular compartment of blood and the majority of studies have only reported plasma or serum concentrations, exposure to this compound is most likely to be underestimated. Clearly this difference in distribution could bias risk assessment where only serum or plasma concentrations of PFASs are considered.

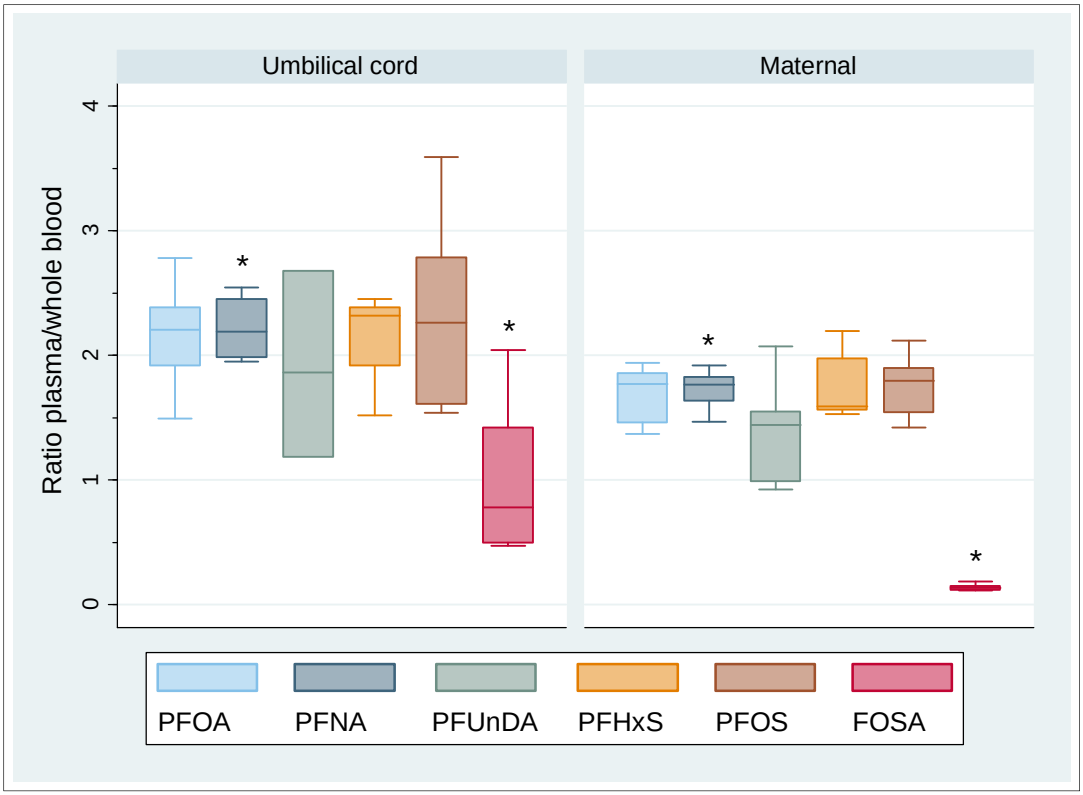


Figure 10. Plasma-whole blood concentration ratios for PFASs in maternal and umbilical cord samples (Norilsk data). The asterisks (*) signifies a statistically significant difference (Wilcoxon signed rank test) between cord and maternal samples. The centre line of the box represents the median and its top (Q3) and bottom (Q1) the 75th and 25th percentiles, respectively; Q3 - Q1 is the interquartile range (IQR); the top and bottom whiskers represent ± 1.5 IQR; and solid circles denote outliers. . (This figure corresponds to Figure 4 of Paper II.)

5.1.3 Comparison of maternal and cord concentrations

As seen in Figures 8 and 9, the placenta seems to function as a partial barrier for PFASs, since the umbilical cord plasma (or serum) concentrations are generally lower than for the mothers for both PFOS and PFOA. Also, and generally speaking, the comparable temporal concentration patterns for the mother and neonate samples in these figures suggest that the geographic dependences and other exposure risk factors discussed for the mothers in Section 5.1.1 appear applicable to the neonates as well. A second general trend in Figures 8 and 9 is that the PFOS concentrations are considerably higher than PFOA. This reflected in both Figure 11 (plasma) and Figure 2 of Paper II (whole blood) since the ratios displayed are less than unity. A closer look at the latter figure indicates that the ratio PFOA/PFOS is considerably higher in umbilical cord than in maternal blood .This is also evident in South

African data set, even though the PFOS concentrations were relatively low and comparable to (maternal serum) or lower than (cord blood) PFOA. This umbilical cord preference for PFOA is explained by a higher transplacental transfer efficiency (TTE) (see below).

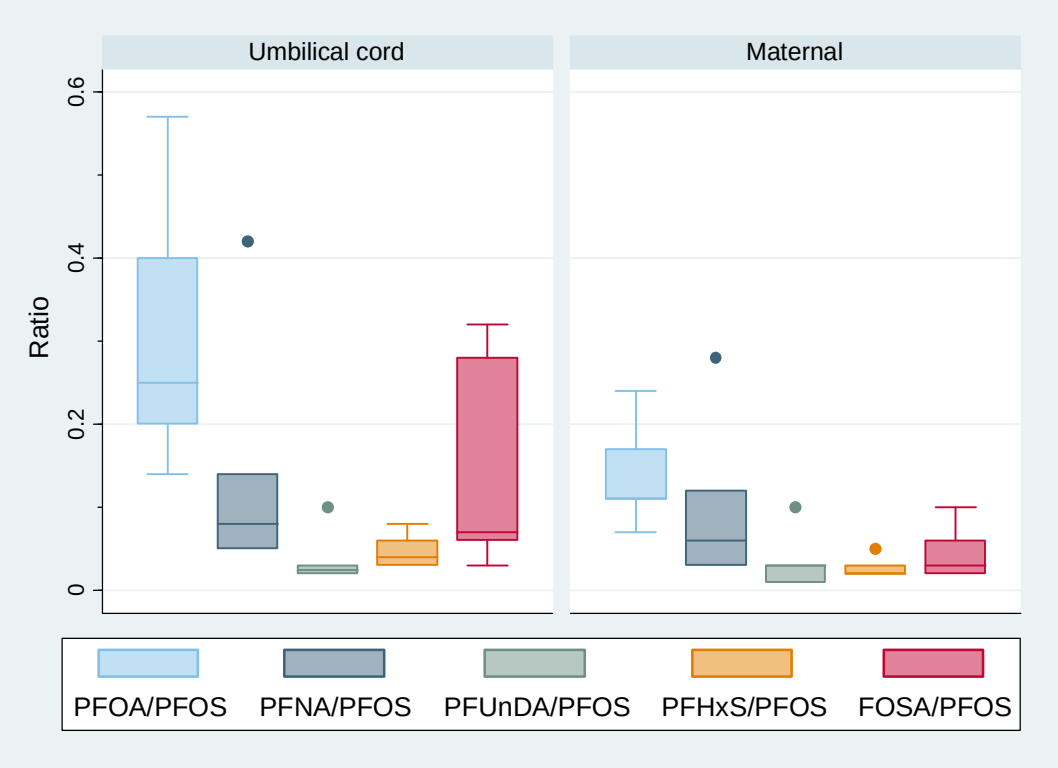


Figure 11. Abundances of PFASs relative to PFOS in plasma (maternal and umbilical cord; Norilsk data). See Figure 10 legend for explanation of the box plot.

Both chain length and functional group are factors that can affect the placental transfer of PFASs. Transport by passive diffusion appears prominent, at least for the majority of anthropogenic compounds (Syme et al., 2004). Transplacental transfer can alter (increase or decrease) during the course of gestation due to changes in placental structure and metabolic demand (Cunningham et al., 2010). As illustrated in Figure 12 by the maternal/cord plasma concentration ratios and in Figure 3B of Paper II for the same whole blood comparison, PFOA seems to cross the placenta more easily than PFOS. The median ratio values for plasma for the anionic PFASs ranged 1.2-2.9 (Figure 12), while those for whole blood for the same compounds were somewhat higher (1.5-3.3; Figure 3B, Paper II); for FOSA, the median values were 0.9 (plasma) and 6.0 (whole blood). Thus the concentrations of all PFASs studied were higher in the mother in both plasma and whole

blood, with FOSA in plasma a possible exception (see discussion below). The maternal-cord concentration plasma ratio has been suggested as a measure of TTE (Beesoon et al., 2011). Apparent increases in this ratio for both plasma and whole blood were evident with the length of the carbon chain for both the carboxylate and the sulfonate PFASs, as observed by others (Beesoon et al., 2011; Gützkow et al., 2011).

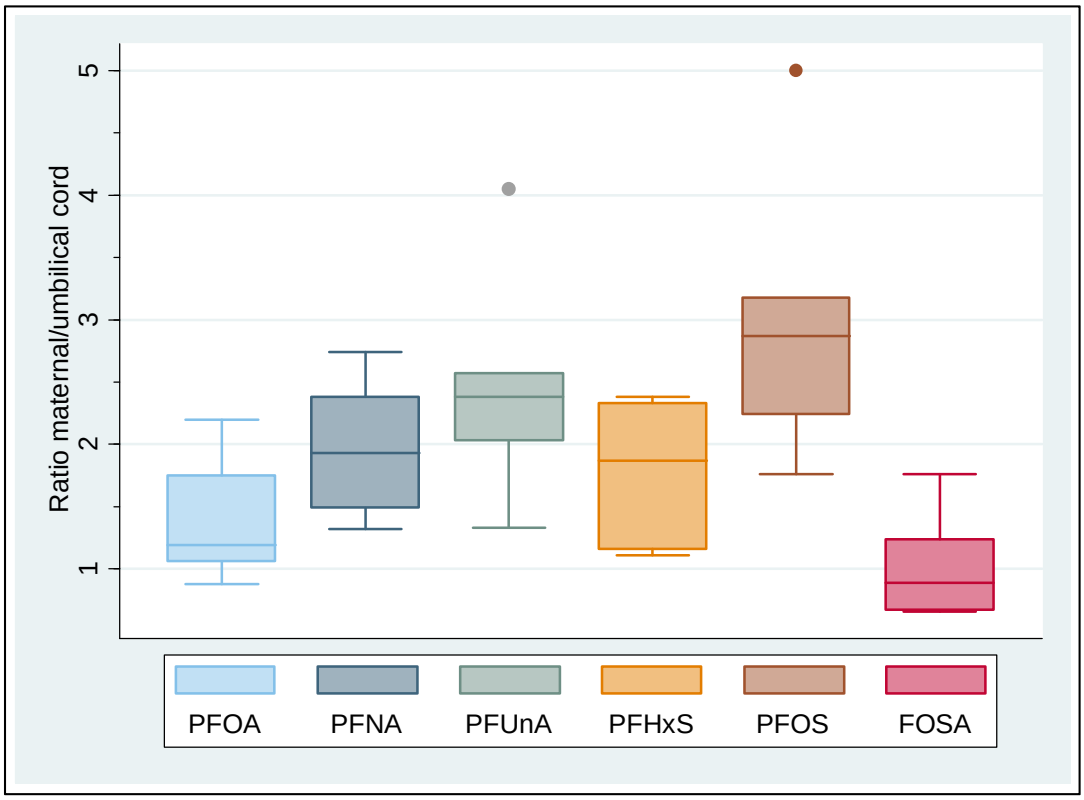


Figure 12: Maternal-cord concentration ratios for PFASs (Norilsk data) in plasma. (This figure corresponds to Figure 3A of Paper II.) See Figure 10 legend for explanation of the box plot.

Clearly FOSA differs from the other PFSAs and PFCAs. It is interesting that for our data set the concentrations of FOSA in whole blood relative to plasma in umbilical cord samples do not favour the former as strongly as is the case for the mother (see Figure 10; also Table 1 of Paper II). Previously reported umbilical cord concentrations of FOSA in serum have been low (the majority of the samples had concentrations below the LOD) (Inoue et al., 2004; Apelberg et al., 2007). Possibly, FOSA's distribution between plasma and the cell fraction of blood is sensitive to the cellular composition of the latter. Indeed the haematological profile of cord blood is quite different; for example, the white cell and reticulocyte counts are quite

elevated (Lewis et al. 2001). Other factors may influence this distribution as well, such as the relatively enhanced levels of certain proteins that occur in cord plasma such as of albumin (Fryer et al.,1993; van den Akker et al., 2008). Further investigation of these observations is warranted.

5.1.4 Relative abundance of linear and branched PFOS

In Paper II, the observed percentages of linear and branched PFOS and FOSA in both whole blood and plasma were comparable (median values between 40 and 50%, see Table 1 in Paper II)). The percentage branched PFOS diverge from the commercially produced products, for which the ratio between linear and branched isomers was 70:30 (Martin et al., 2010). Our observation suggests that the increased percentage of branched PFOS reflects increased branching of the FOSA precursor, and that some of the PFOS exposure is due to biotransformation of precursor compounds (Benskin et al., 2009b).

Although a precursor to PFOS, FOSA itself is a degradation product of Et-FOSE and Et-FOSA (Xu et al., 2004; Benskin et al., 2009 b), Et-FOSE/FOSA were produced exclusively by the ECF process and consists of both branched and linear isomers in unequal proportion (the linear form is most prevalent). The biotransformation of Et-FOSE to FOSA is quite rapid (Fromme et al., 2009) and there is a preferential biotransformation of branched Et-FOSA (Benskin et al., 2007). This might explain the increased percentage of branched PFOS reported in several studies (Kärrman et al., 2007a; Haug et al., 2009; Rylander et al., 2009). Published FOSA concentrations in serum or plasma have been low and, as we point out, more likely underestimated. Consequently, the percentage branched FOSA could have been difficult to estimate.

The proportion of branched PFOS in umbilical cord samples was addressed both in Papers I and II. In Paper I, we report a higher percentage branched PFOS in cord blood (48%) (corrected for cell displacement) compared to maternal serum (42%). This is in accordance with a study where a more detailed isomer identification was performed (Beesoon et al., 2011). In Paper II maternal samples had higher percentage of branched PFOS, both in plasma and whole blood (respectively, 49 and 53%), compared to cord samples (42 and 47%). These results could have been biased by instrumental limitations (UPLC-MS-MS *versus*. LC-QToF)

and time of sampling of maternal blood, but an influence of geographical exposure differences, such as direct and indirect exposure, cannot be discounted.

5.2 Human Biomonitoring of cVMS

5.2.1 Observed concentrations in perspective

As indicted in Section 1.4.3, only a few human biomonitoring studies have looked at cVMS concentrations in human plasma. For the first time, we reported cVMS concentrations in plasma from women randomly selected from the general population. The most prominent compound was D4 followed by D5 and then D6; however the latter two were not reported for the MISA cohort. The median D4 plasma concentrations for the NOWAC and MISA cohort were respectively 4.80 and 2.07 ng/mL. This is somewhat higher than reported for ten controls in the study by Flassbeck et al. (2001), where no cVMS were reported above the detection limit (2 ng/mL). Flassbeck et al. investigated the cVMS content in blood plasma of women with breast implants. They reported D4 as the most prominent compound with concentrations ranging from 2 to 50 ng/mL. In a recently published study, cVMS and linear siloxanes concentrations were reported in blood plasma from current and previous cVMS production facility workers and people living near the plant (Xu et al., 2012). In current workers, both D4 and D5 were reported with average >200 ng/g (detection frequency was 100%). A linear siloxane was the most prominent compound in this group (median >400 ng/g). In the control group (community perpendicular to the wind direction of the plant; n=58), D4 and D5 were reported in two and three samples respectively with concentrations ranging from 1.2-3.6 ng/g (D4) and 2.0-5.0 ng/g (D5). This is comparable to that for our NOWAC women, for whom the median concentrations for D4 and D5 were 4.80 and 1.94 ng/mL respectively. It is worth to mention that in both the study by Flassbeck et al. (2001) and Xu et al. (2012), the cVMS exposure is not applicable to the general population.

Compared to PFASs and legacy POPs, cVMS differ in exposure routes as already indicated in Section 1.4.3. Rather than diet, dermal application and inhalation would be the major exposure pathways. The low detection frequency of cVMS in the samples from the MISA pregnant women together with the small number of participants complicates comparisons between the two groups. Nevertheless, some discussion still seems warranted.

The NOWAC estimated exposures to cVMS are comparable to the amounts applied by United States women in body lotions (respectively, 7.4, 4.0 and 1.0 µg/day for D4, D5 and D6, respectively; Horii and Kannan, 2008). By contrast, the estimates by these authors of the total D4, D5 and D6 applied in personal care and cosmetics products show quite an unrelated pattern (1 080 , 233 000 and 22 000 µg/day, respectively). Dermal absorption rate is likely an important determining factor: D4 (0.5 %) > D5 (0.04 %) ≈ D6 (estimated at 0.1 %) (see Section 1.5.2). It should be reiterated that prior to the sampling of the NOWAC plasma samples, the amount of cVMS registered in Norway was at its maximum (see Figure 13), followed by a sharp decline in 2005. This pattern may nevertheless imply that exposures were potentially higher for the NOWAC women. However, this figure is incomplete since cosmetics containing cVMS were not included in it, and may therefore underestimate important potential exposures for the 2005-2009 study period.

The difference in age between the cohorts (up to 30 years) may also be relevant. Changes in skin are a natural consequence of age, and this might lead to a alterations in the permeability of chemicals through the skin (Poet and McDougal, 2002; Farage et al., 2008). Perhaps higher use of PCPs by the older NOWAC group occurred, or that pregnant women are more cautious with respect to use of such products. We cannot disregard the possibility that MISA women historically might have had elevated concentrations.

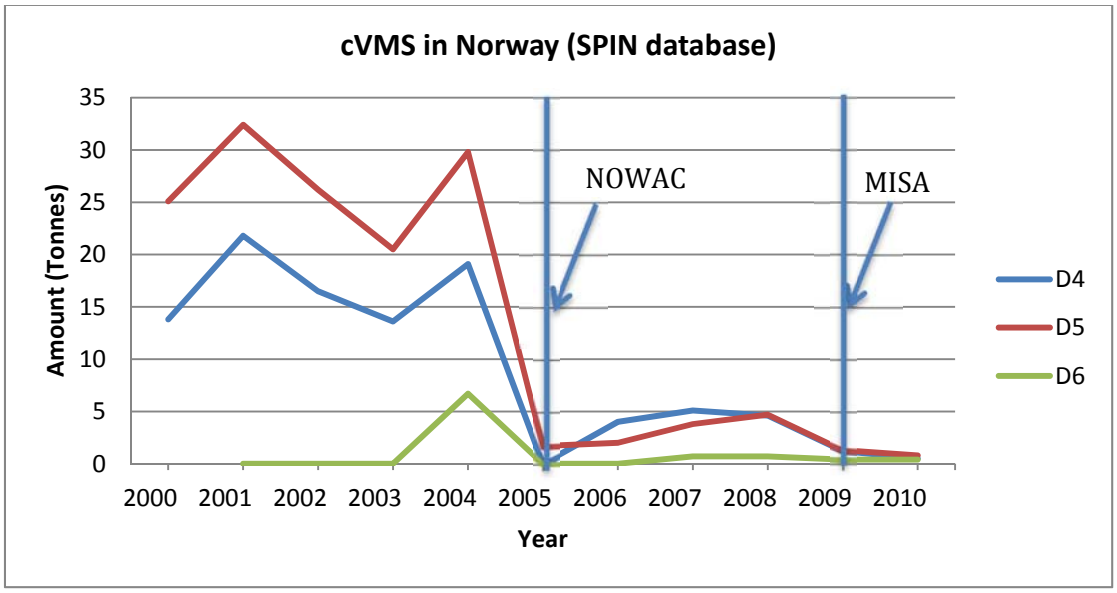


Figure 13: Sampling year for NOWAC and MISA cohort and registered imported cVMS in Norway.

cVMS exposure risk factors such as breast implants and PCPs use were assessed by questionnaires in the NOWAC cohort. As pointed out in Paper III, there was no statistically significant trend for the investigated cVMS with respect to daily percentage body surface area creamed. Nevertheless, and as indicted in Figure 14, the median D4 concentrations increased with the percentage of area skin creamed, however this observation was not statistically significant. The absence of breast implants was assessed only for the NOWAC subgroup. Lack of extreme values observed for the MISA women suggests their absence or, as a minimum, none of possible implants was leaching.

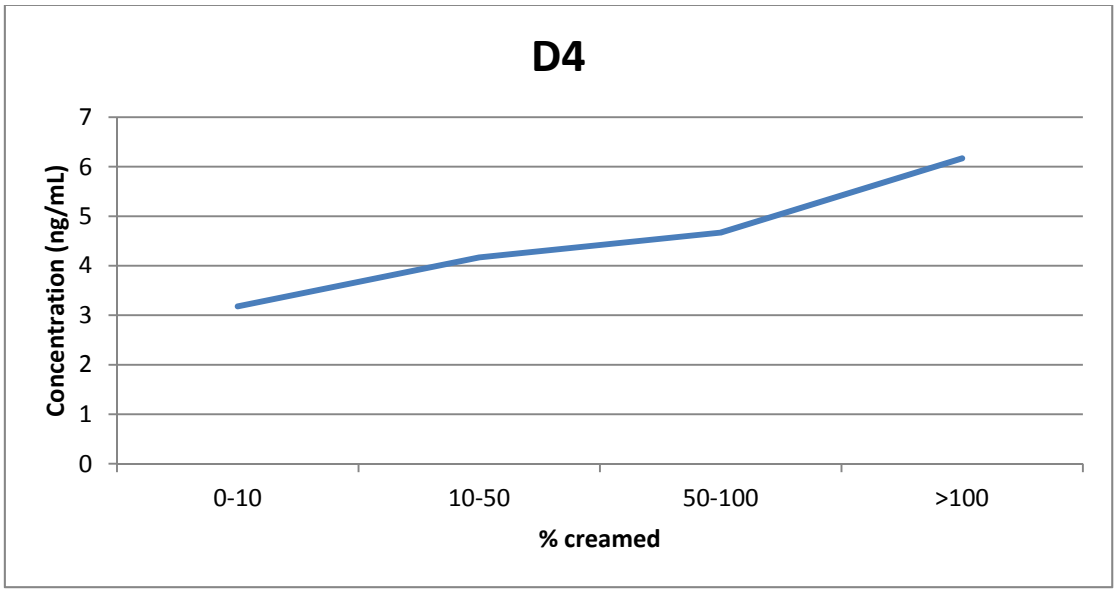


Figure 12. Percentage of area skin creamed *versus* median concentration of D4 in the NOWAC cohort (p = 0.12).

As indicated in Section 5.3.3.2, the ubiquitous presence of cVMS in the laboratory was a challenge with respect to conducting the analytical chemistry. In spite of rigorous quality assurance steps, the LOQs were rather high (1-2 ng/mL of plasma). It is interesting to note that this concentration is two-to-three times higher than those reported for PCB 153 (AMAP, 2009, revised 2012). Some concern remains therefore about cVMS exposures experienced by humans. Furthermore, the short turnover time for cVMS in the body due to their rapid metabolism and excretion (as described in section 1.5.2) could lead to bias with respect to exposure doses, since a plasma sample in the morning could differ from one in the afternoon.

5.2.2 Blood matrices

Both plasma and whole blood seemed to be suitable matrices. [Use of serum was not possible due to inadverted contamination from the collection tubes (see Section 5.3.3.2)]. One study (Flassbeck et al., 2001) reported higher concentrations in whole blood compared to plasma, however the samples were not paired. In paired samples (n=2) we found comparable concentrations in the RBC fraction compared to the plasma samples, however due to the low detection frequency and a small number of participants it was not possible

to confirm the observations by Flassbeck et al. (2001). Whole blood as an alternative matrix for cVMS determination should be investigated further. Based on the observation that D5 in animal studies has shown a preference for storage in fat, plasma or whole blood might be the most suitable medium. They would be the perferred over urine because D4 and D5 have common metabolites (Varaprath et al., 1999, 2003).

5.3 CHALLENGES AND LIMITATIONS

5.3.1 Preamble

For HBM studies to have an impact, their results must be trustworthy and have validity. This is ensured by good study design, quality assurance and quality control procedures. Below challenges and limitations relevant for the cohorts presented in this thesis are discussed.

5.3.2 Study design, sample size, and external validity

In total, five populations are included in the three thesis research papers: delivering women from South Africa, Uzbekistan and from Norilsk in Russia; pregnant Norwegian women (MISA); and postmenopausal Norwegian women (NOWAC). The common denominator is that all studies have a cross-sectional study design.

For both the original NOWAC and MISA cohorts, the external validity have been discussed (respectively, Lund et al., 2003; Hansen, 2011). Since the number of participants from the MISA cohort in Paper III was by necessity rather low, therefore so is the external validity. On the other hand, the external validity for the cVMS findings for the NOWAC women may be rated as good, as this cohort has been shown to be representative of Norwegian women of the same age (Lund et al., 2003). As the NOWAC study was not designed to study PCP use, bias in terms of product use and pre-selection of women choosing to participate was avoided (Sandanger et al., 2011).

No formal validation of the external validity of South Africa, Russia and Uzbekistan cohorts was conducted. The low number of participants from Russia and Uzbekistan made such validation difficult.

5.3.3 Quality assurance and control (internal validity)

5.3.3.1 PFASs

Early reported PFAS concentrations varied widely, and several laboratory round-robins were conducted and reported on to resolve underlying analytical challenges. The results of such efforts have been published in the peer-review literature, including validation of clean-up methods (Reiner et al., 2011). In consequence, the following modifications have helped to decrease uncertainty in PFAS analyses: increased number of mass-labelled standards; better analytical instrumentation; and awareness of inadvertent contamination from multiple sources [e.g., equipment containing PTFE (e.g., Teflon) tubing; and co-elution of compounds naturally present in the analytes (e.g., bile acid; Benskin et al., 2007)]; and use of standard reference materials. Today the variation is ± 20% or better (Lindström et al., 2009; Reiner et al., 2011), which is acceptable. Our results from analysis of standard reference materials (SRMs) and participation in round robbins are well within this variation.

The quantification of branched PFOS and FOSA in Paper II has some limitations. The quantification transition used for linear PFOS (499→80) is not representative for all of the different branched isomers (Berger et al., 2011). Since the isomers are not separated, and no separate response factor was calculated for them, there is a possibility of either under or overestimation. This discrimination was not apparent in Paper I, since the analysis was done on a QToF instrument and the molecular ion was used in quantification. For FOSA, no branched isomers are commercially available, which made the isomer quantification in Paper II less significant. However, and as suggested by Benskin et al. (2010), analysis of a technical mixture can be used as a guideline for estimating the percentage branched. Our comparison of the various FOSA profiles (see Supplementary Data Figure S1 of Paper II), provided confirmation of the increased amount of branched FOSA in whole blood samples.

5.3.3.2 cVMS

cVMS analyses were more challenging than PFASs, especially with respect to inadvertent contamination and the high volatility of the these compounds. Serum tubes proved to be unsuitable due to the "gel" in the tubes that contained large amounts of cVMS. The presence of cVMS in PCPs led to initiatives to minimize inadvertent contamination during clean-up and analysis, including curtailing personal use. Consequently, we carried out all sample

clean-up activities in a clean room facility. To minimize instrumental background, the analyses were carried out in the late afternoon of work days and during weekends when the human activity in the laboratory was low. To lower the background further, we selected a low bleed GC-column (DB WAX ETR) and chose a conservative approach to LOQ calculation in response to the multiple indavertent sources of contamination identified. Additional precautionary measures adopted during sample preparation are described in Paper III. The external validation of the cVMS clean-up and analysis have been established in two round-robin published exercises (McGoldrick et al., 2011; Warner et al., 2012).

As alluded to in Section 5.2.2, an unexpected pitfall was encountered. The analysis of serum collection tube washings (BD Vacutainers, SST II Plus Advance 10/8.5 ml) showed that contamination had occurred. Rinses had high concentration, typically: D4 (111 ng/mL), D5 (200 ng/mL) and D6 (199 ng/mL) whereas no cVMS was present in similar washings from the plasma vacutainers used subsequently.

5.3.4 Storage

5.3.4.1 PFASs

Berger et al. (2011) showed that the recovery of longer chain PFCAs dissolved in water (PFUnDA and PFDoDA) decreased during a storage period of 90 days when were stored in polypropylene (PP) bottles at 4°C. Other PFSAs and PFCAs did not show similar behaviour. This observation may have implications for the long-term storage of surface active compounds such as PFASs. To which degree storage has had an impact on the samples analysed in Papers I and II is unknown. All of the plasma samples were stored at -20°C until extraction and before analysis. Before an aliquot was taken out, the sample tube was thoroughly shaken. The binding of PFCAs to proteins, for example, would likely lower their adsorption onto the storage container walls. In a study from the U.S, samples were reanalysed after several years of storage at -80°C, and there was no statistical differences in either PFOS or PFOA concentrations (Olsen et al., 2007b). This indicated that long term storage at low temperatures appears not to be a problem.

5.3.4.2 cVMS

No studies with respect to long-time storage of samples, as described for PFASs, have been conducted for cVMS. However, the high vapour pressure of cVMS is challenging in environmental exposure studies (Brooke et al., 2009b). In a study by Krogseth et al. (2013), cVMS concentrations on spiked passive-air sample disks did not decrease after 30 days storage at - 20°C. The high fat:blood partition of cVMS (Reddy et al., 2008), which reflects their low water solubility, suggest that cVMS may be even more protected from vaporization when in plasma or serum. We expect that very little loss of cVMS occurred in our samples.

6. CONCLUDING REMARKS

- A literature review of cross-sectional studies showed that sampling year is an important predictor of plasma PFAS concentrations (a decrease with time has occurred since phase-out).
- Exposures to PFASs depends on where you live, and in this study concentrations were decreases in the order: remote Arctic Russia, South Africa and Uzbekistan.
- Compared to the other PFASs studied, the relatively high pK_a value of FOSA, which is a physicochemical acid-base property, appears to explain its unique distribution between plasma and the cellular fraction of blood. Whereas ionic PFASs reside in the plasma fraction, the majority of FOSA are in the cellular fraction.
- The experimental data suggests that the placenta acts as a partial barrier for PFASs, with long chain PFASs being more retained than short chain homologs and PFSAs more than PFCAs.
- cVMS concentrations are reported for the first time in Norwegian females randomly selected from the general population.
- The ubiquitous presence of cVMS in the laboratory environment constitutes an analytical challenge.
- Even though the observed cVMS concentrations were close to the detection limit, their absolute magnitude exceeded those for certain legacy POPs. Therefore, some concern about their presence in the environment and humans remains.
- The results from the two cohort studies (MISA and NOWAC) can be used for the exposure component of human health risk assessment of the compounds investigated.

7. Future Perspective

HBM can be time consuming, expensive and requires relatively large sample volumes. This is still an issue for monitoring children (including use of the umbilical cord). The challenge to overcome this shortcoming requires the continued development of more sensitive analytical methods (i.e., lower LODs) and supporting small-sale sample preparation technologies.

Vital information can become lost in the search for new contaminants in HBM studies if the matrices of choice are not optimum for the compounds in question. The current work has demonstrated that whole blood measurements are essential for estimating the exposure to selected PFASs and matrix selection is therefore important for the monitoring of emerging contaminants.

Compounds in PCPs (parabens and siloxanes) are metabolised quite rapidly in humans and time of sampling compared to the exposure time could create bias. The timing of specimen collection is therefore crucial. Another challenge for substances that are in wide use such as the PCPs is inadvertent contamination as demonstrated for CVMS. Other examples are: phthalates, bisphenol A, parabens, and linear siloxanes. Working in clean rooms is required, and this would limit the number of laboratories able to carry out reliable analytical work involved in HBM

A long standing issue has been how to assess the combined effects of multiple environmental contaminants. Compared to 10 years ago new instrumentation and techniques has led to a vast list of compounds and over 200 known contaminants are present in human blood. A fair question is how will long term exposure to contaminant cocktails affect the general population? The number of diseases in which contaminants potentially may play a role is increasing in prevalence. This warrants further studies on the connection between contaminants and human health. New ways of exploring cause and effect are needed. One future perspective might involve a combination of HBM of exposure and of effect such as the new approach referred to as “exposome” technology (e.g., use of genetic expression). It is thought to be able to capture an assessment of the total exposure experienced and aspects of its effect. We are only seeing the beginning of this new scientific endeavour and there is a long way to go (Rappaport and Smith, 2010; Rappaport, 2012; Vineis et al., 2013).

And finally, a consortium to coordinate and harmonise approaches to HBM in Europe has been established. This can be an important tool to effectively monitor both exposure to chemical substances and address potential health effects they incur (http://www.eu-hbm.info/cophes).

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ERRATA

Paper II:

Discussion: An important difference between our work and that by Beesoon et al. (2011) and Gützkow et al. (2012) is time of sampling during pregnancy (respectively at delivery, week 15 and week 37).

In the study by Gützkow et al.(2012), informed consent was collected in week 37 whereas the blood sample was collected immediately after delivery.

Supplemental: In Table S3: PFUnDA concentration in cord plasma for id code 27 is in the table set as 0.02 ng/mL. The correct value should be < 0.05 ng/mL.

Paper III:

2.2 Sample extraction: tris(trimethylsilyloxy)silane is misspelled and should have been written; tris(trimethylsiloxy)silane.

Paper I

Paper II

Paper III

APPENDIX I

Basis for Paper I

Questionnaires

MEDICAL RESEARCH COUNCIL

ENVIRONMENT & REPRODUCTIVE HEALTH STUDY

This questionnaire is part of the Medical Research Council environment and reproductive health study. We would like to request that you take the time to answer the questionnaire with the assistance of trained interviewer. We thank you in advance for your participation.

If you have questions or need more information, please do not hesitate to call Dr Halina Röllin at 011 274 6064(office hours).

SUBJECT STUDY NUMBER …… **AREA STUDY CODE…….**

Clinic Name: ......

Clinic address: …….....

Town/Province: ……

Interview date (date/month/year): .....

Interviewer: …….....

SECTION A: BACKGROUND DETAILS

In this section we would like to obtain a few background details about yourself.

1. What is your first name? .....……

2. What is your surname? .....…….

3. What is your home address?.....

   .....

   .....

4. What is your present contact telephone number
   ……

5. When were you born? (please give day, month and year)

   Where……

   Day ……

   Month ……

   Year …….

6. How many children do you already have:

   ……

7. How many daughters do you have: number: …… ages: …….

8. How many sons do you have: number: ……..ages ……..

9. What language do you usually speak at home (**please circle!**)

   1. English
   2. Afrikaans
   3. Xhosa
   4. Sotho
   5. Zulu
   6. Other (please specify) …….

10. What is your race/population group? (**please circle!**)

(This question is being asked because in South Africa population group is still closely linked to economic status, which in turn is closely linked to certain environmental factors.)

1. African black
2. Coloured
3. Asian
4. White

11. What is your nationality? …….

12. How would you describe your place of residence **(please circle one answer only)**

1. Urban (city)
2. Rural (farming community)
3. Peri urban (close to the city)
4. Informal settlement
5. Close to industrial site: (please specify) ……
6. Don't Know

13. How long have you lived at your present home address?

Years ……

Months ……

SECTION B: HOUSING

In this section we would like to have some information about the household you presently live in

1. Is this home: **(please circle)**

    1. Owned
    2. Rented

2. How would you describe your home? **(please circle)**

    1. House
    2. Flat
    3. Backyard dwelling
    4. Informal house (shack)
    5. Other (please specify) .....

3. How many rooms, not counting the kitchen, bathroom or toilet, does this home have? ……

4. What fuel is used most of the time for cooking? **(please circle)**

    1. Electricity
    2. Paraffin
    3. Gas
    4. Wood
    5. Coal
    6. Car batteries
    7. Other (please specify) .....……..

5. What fuel is used **most** of the time for heating the home? **(please circle)**

    1. Electricity

2. Paraffin

3. Gas

4. Wood

5. Coal

6. Car batteries

7. None

Other (please specify) .....

6. Does anyone regularly smoke at home? **(please circle!)**

1. Yes

2. No

7. How many people regularly smoke cigarettes in the home? (At least one cigarette per day at home)
.....……

8. Did you smoke: **(please circle)**

1. Before pregnancy

2 During pregnancy

3. Both

4. Number of cigarettes daily

9. Where do you get your drinking water from most of the time? **(please circle)**

1. Indoor tap

2. Outdoor tap

3. Rainwater tank

4. Borehole

5. River/stream

6. Other (please specify)…….

SECTION C: SOCIAL AND ENVIRONMENTAL ASPECTS

In this section we will ask some questions relating to you and other people living in your home.

1. Marital status: **(please circle)**

    1. Married
    2. Divorced
    3. Single
    4. Living together
    5. Widowed

2. How many people live in this house?

    1. Males older than 15 years
    2. Women (including yourself) older than 15 years
    3. Children aged 15 years or younger

3. What is your highest educational qualification?

    …….. .....

4. Do you have permanent job: **(please circle)**

    1. YES
    2. NO

    If yes, what type (seasonal or pemament) **please underline**

    Employer……..

    Occupation/Position……..

5. For how many years have you held your current job?

    …….

6. What does your husband/partner do at work?
……..
……
……

7. Where does he work?
……..
…….

8. What is the highest education qualification of your husband/partner?
…….. .....

9. How many years has he held his current job?

…….

10. How many people, living with you, have permanent jobs?
…….

11. Does anyone living in the house, work from home? (please circle)

    1. Yes
    2. No
    3. Don't know

    If yes, what do they do?

.....…….
…….

12. If maintaining or repairing your home, do you or handyman use lead-containing materials (paints, solders etc).? **(please circle)**

    1. Yes
    2. No
    3. Don't know

13. What is the total monthly income in your family?

.....

14. Describe the hobbies of people living in the house (for instance car repairs, pottery, welding, etc).

……

……
……

15. What is your opinion on air quality in your area? **(please circle)**

    1. Good
    2. Bad
    3. I don't know

16. Are there any sources of environmental pollution around your home? **(please circle)**

    1. Yes
    2. No
    3. If yes specify source ,……

    …….

17. How far is your home from the nearest the highway? …. .**Km**

18 Do you use pesticides for insect control (flies, bugs, cockroaches, mosquitoes, in your home?) **(please circle)**

    1. Yes
    2. No

19. If yes, are these pesticides used in: **(please circle)**

    1. Kitchen
    2. Living room
    3. Bedroom
    4. Others, please specify

    ……

20. What are the names of the pesticides do you use?

    ……..

21. How often do you use the pesticides?

    1. In a week

2. In a month

22. Where do you store these pesticides? ……

23. Do you grow your own food? (vegetables, fruits, others) **(please circle)**

1. Yes
2. No

If yes specify……

24. Do you use pesticides in you garden? **(please circle)**

1. Yes
2. No

If yes please specify which pesticide?
…….

25. Do you or a member of your household fish? **(please circle)**

1. Yes
2. No

Where do you fish? Please name the location …….

Please name the fish type ……

26. If yes do you consume this fish? **(please circle)**

1. Yes
2. No

27. Is your house sprayed regularly by Malaria Control Programme

1. Yes……
2. No

If yes how often…….

28. Is the crop at farms near your house sprayed.

1. Yes
2. No

SECTION D: INFORMATION ABOUT YOUR JOB

Please list in chronological order all the jobs you were engaged in for the period of more than 6 months, over the past 10 years. Also mention whether you were exposed to any chemicals during your work (which):

JOB DESCRIPTION AND WHERE	FROM	TO	DO YOU KNOW OF ANY CHEMICALS USED AT YOUR WORK PLACE

Chemicals check list (please circle Y/N)

1	Solvents (turpentine, spirits, paraffin,	Yes	No
2	Paints	Yes	No
3	Metals (in foundry, mine	Yes	No
4	Cleaning fluids (floor, windows	Yes	No
5	Polish (for floor, car polish	Yes	No
6	Paint removers	Yes	No
7	Oils/lubricants (grease….)	Yes	No
8	Spray paints	Yes	No
9	Spray oils	Yes	No
10	Others, please specify	Yes	No

SECTION E: HEALTH

In this section some information about your health status is requested.

1. Are you well at present?

    1. Yes
    2. No
    3. Don't know

2. If you are not well, what are the problems?

    ….....……

    ….....……

3. Do you suffer from any of the following? (**circle correct answers please)**

    1. Diabetes

        Since when / How long ……..

        Are you on medication for this condition? YES NO

    2. Thyroid gland

        Since when / How long ……..

        Are you on medication for this condition? YES NO

    3. Liver disease

        Since when / How long

        Are you on medication for this condition? YES NO

    4. Heart disease

        Since when / How long

        Are you on medication for this condition? YES NO

    5. High blood pressure

        Since when / How long

        Are you on medication for this condition? YES NO

    6. Infectious/parasite disease, **if yes please tick:**

1. TB (tuberculosis)

2. Pneumonia

3. Virus hepatitis

If other please specify ……..

7. Cancer YES NO

If yes, please specify …….

If yes, did you receive treatment: ……..

Please specify type of treatment…….

8. Are there any hereditary diseases in family (for example high blood pressure, lung disease, etc.?)

If yes, please specify ……..

9. Do you suffer from any other illnesses (for example skin condition etc):

1. Yes

2. No

If yes, please specify)….....

10. Have you ever been given any home remedies for illnesses or to improve your health (please circle)?

1. Yes

If yes, please specify……..

2. No

3. Don't know

11. Are you taking any prescription medication at present? (please circle)

    1. Yes:

    If yes, what medication are you taking, please specify:

    ……..

    ……

    2. No

    3. Don't know

12. Are you taking any special remedies during your pregnancy?

    If yes, please specify ……

    ……

13. How long did you breastfed your other children:

    1. Child 1 (oldest)……..

    2. Child 2…….

    3. Child 3…….

    4. Child 4……

    5. Child 5…….

14. Do you plan to breastfeed this child:

    1. Yes

    2. No

SECTION F: DIET AND LIFESTYLE

Please answer questions about your usual diet before and during pregnancy:

Table: Frequency of consumption of food / before / during pregnancy,
1 =seldom; 2= at least once a week; 3-= almost every day

TYPE OF FOODSTUFF	**BEFORE PREGNANCY**	**DURING PREGNANCY**	**FOOD LOCALLY PRODUCED (by respondent or in the area) Y/N**
PROTEINS			
Meat			
Poultry			
Processed meet (smoked sausage, ham etc)			
Tinned meat			
Eggs			
Fish fresh			
Fish tinned			
Fish smoked			
Sea food			
VEGETABLES AND FRUITS			
Vegetables root (potatoes, carrots, beetroot, onion etc)			
Vegetables leafy/ground (spinach, cabbage, lettuce, cucumbers, pumpkin, water melon etc)			
Vegetables vine/tree (mielie, beans, tomatoes, garlic)			
Fruits			
DAIRY PRODUCTS AND FATS			
Dairy products (milk)			
Butter and cheese			
Fats (oil, margarine)			
CARBOHYDRATES			
Cereals (mieliepap,rice,noodles)			
Bread			
Sugar			
FLUIDS			
Fresh fruit juices			
Soft drinks			
Bottled water			
NON FOOD			
Non food items specify			

2. How many cups of coffee do you drink?

    1. Daily

    2. Weekly

3. How many cups of tea do you drink?

    1. Daily

    2 . Weekly

4. How many bottles of beer do you drink?

    1. Weekly

    2. Monthly

    3. None

5. How many bottles of wine do you drink?

    1. Weekly

    2. Monthly

    3. None

6. How many glasses of vodka or other strong alcohols do you drink?

    1. Weekly

    2. Monthly

    3. None

7. Do you smoke?

    1. Yes

    2. No

8. If yes, for how many years have you smoked regularly? ……**years**

9. At what age did you start to smoke regularly? …….

10. What do you smoke? **(please circle)**

    cigarettes self-rolled cigarettes pipe cigars

11. How many cigarettes do you smoke daily?.....

12. If you do not smoke, did you smoke earlier? Yes No

13. At what age did you start to smoke regularly?.....

14. At what age did you quit smoking? …….

15. Within the last 6 months, did you take any drugs that influenced on your mood?

    1. Yes
    2. No
    3. Refused to answer

16. Do you have any hobby?

    1. Yes
    2. No
    3. If yes, what?

17 How many times you visited this clinic during pregnancy:……

END OF QUESTIONNAIRE,
THANK YOU for answering the questions, your assistance is highly appreciated.

APPENDIX II

Basis for Paper II

Questionnaires

МОРСКАЯ ПИЩА И ЗДОРОВЬЕ НАСЕЛЕНИЯ СЕВЕРА

Вы согласны принять участие в исследовании?
Да ☐ Нет ☐

Место жительства: .....
населённый пункт

Дата I _ I _ I I _ I _ I I _ I _ I _ I
день месяц год

Инициалы I _ I _ I _ I

Ф И О (**Ф**амилия, **И**мя, **О**тчество)

Идентификационный номер участника .....

Объективные данные

Время измерения I _ I _ I часов

Артериальное давление

Измерение	Систолическое артериальное давление	Диастолическое артериальное давление
1	..... мм рт. ст.	..... мм рт. ст.
2	..... мм рт. ст.	..... мм рт. ст.
Среднее	..... мм рт. ст.	..... мм рт. ст.

Частота пульса

Измерение	Частота пульса
1	..... уд./мин.
2	..... уд./мин.
Среднее	..... уд./мин.

Антропометрия

Рост ....., см
Вес ....., кг
Окружность талии ....., см
Окружность бёдер ....., см
Индекс массы тела ..... вес кг / рост м2
Окружность талии/ Окружность бёдер ..... см

Забор крови

Время взятия крови I _ I _ I часов

Взятие крови натощак Да ☐ Нет ☐

Сколько времени прошло с последнего приёма пищи? I _ I _ I часов

Что Вы кушали, пили в последний приём пищи?

1 ..... 2 ..... 3 .....

4 ..... 5 ..... 6 .....

Употребляли ли Вы спиртные напитки вчера или сегодня? Да ☐ Нет ☐

Анкета

Личные сведения, социальное положение

Возраст I _ I _ I лет

Дата рождения I _ I _ I I _ I _ I I _ I _ I _ I
день месяц год

Пол Мужской ☐ Женский ☐

Какое образование Вы получили? (Выберите только один вариант ответа)

- Обучение традиционным навыкам и знаниям вне школы ☐
- Неоконченная начальная школа ☐
- Начальная школа ☐
- Неполная средняя школа 9 кл. (или 7-8 кл.) ☐
- Полная средняя школа 11 кл. (или 10 кл.) ☐
- Среднее профессиональное образование (техникум, училище, колледж) ☐
- Неоконченное высшее образование (университет, институт), если 3 года и более ☐
- Оконченное высшее образование (университет, институт) ☐
- Аспирантура после университета, института (диплом кандидата, доктора наук) ☐

Какую работу Вы выполняете (выполняли) или по какой специальности Вы работаете (работали) большую часть Вашей жизни?

должность .....

место работы .....

Я не работал(а) ☐ Не знаю, нет ответа ☐

Какая у Вас была основная работа или способ заработать на жизнь последние 12 месяцев?

должность .....

место работы .....

Я не работал(а) ☐ Не знаю, нет ответа ☐

Вы сейчас? (Выберите да или нет в каждой строке)

	Да	Нет
Работаете по найму полный рабочий день за плату	☐	☐
Работаете по найму неполный рабочий день за плату	☐	☐
Работаете не по найму, частный предприниматель	☐	☐
Домохозяйка	☐	☐
Неработающий пенсионер	☐	☐
Учитесь	☐	☐
Безработный(я)	☐	☐
Не способны работать вследствие инвалидности, проблем со здоровьем	☐	☐
В отпуске по беременности и уходу за ребёнком	☐	☐

Сколько лет Вы живете в этой северной местности?

I _ I _ I лет **(Если меньше, чем 12 месяцев, укажите 00)**

К какой этнической группе могла бы отнести себя Ваша мать? (Выберите только один вариант ответа)

- Аборигенные народы Севера («чистокровная» ненка или представитель другого северного этноса) ☐
  _____
- Неаборигенные народы (русские или др. национальность) ☐
  _____
- Смешанная группа (аборигенные и неаборигенные народы Севера) ☐
- Не знаю, нет ответа ☐

К какой этнической группе мог бы отнести себя Ваш отец? (Выберите только один вариант ответа)

Аборигенные народы Севера («чистокровный» ненец или представитель другого северного этноса) ☐
_____

Неаборигенные народы (русские или др. национальность) ☐
_____

Смешанная группа (аборигенные и неаборигенные народы Севера) ☐

Не знаю, нет ответа ☐

В соответствии со свидетельством о рождении, паспортом, другими документами Вы относитесь к...?

Русским ☐ Украинцам ☐ Белорусам ☐

Ненцам ☐ Коми ☐

Другой национальности, пожалуйста, охарактеризуйте какой ☐↓

.....

Не знаю, Нет ответа ☐

По собственному мнению и ощущениям Вы относитесь к…?

Русским ☐ Украинцам ☐ Белорусам ☐

Ненцам ☐ Коми ☐

Другой национальности, пожалуйста, охарактеризуйте какой ☐↓

.....

Не знаю, Нет ответа ☐

Вы (выберите только один вариант ответа):

Замужем/женат ☐ Живете вместе ☐ Разведен(а) ☐

Никогда не были замужем/женаты ☐ Вдова/вдовец ☐

Сколько человек, <u>включая Вас</u>, в возрасте старше 18 лет живут в Вашем доме?

Число I _ I _ I

Сколько детей младше 18 лет живут в Вашем доме?
Отметьте 00, если нисколько.

Число I _ I _ I

Сколько человек в Вашей семье получают доход?

Число I _ I _ I

Сколько составляет совокупный ежемесячный доход на каждого члена Вашей семьи в среднем, включая все источники: зарплаты, пенсии, пособия, стипендии, др.?

Менее чем 1500	☐	1500,1-2500	☐
2500,1-3500	☐	3500,1-4500	☐
4500,1-6000	☐	6000,1-8000	☐
8000,1-12000	☐	Более чем 12000	☐

Не знаю, нет ответа ☐

Питание

Являетесь ли Вы вегетарианцем (не употребляете мясо в пищу, но употребляете курицу и рыбу)?

Да ☐ Нет ☐

Соблюдаете ли Вы диету в настоящее время?

Да ☐ Нет ☐

Если да, какая это диета?

.....

Если да, как долго Вы соблюдаете диету? (Впишите количество лет, месяцев):

I _ I _ I лет I _ I _ I месяцев

Вы (отметьте ниже Да или Нет по каждому пункту):

Страдаете сниженным аппетитом
Да ☐ Нет ☐

Страдаете повышенным аппетитом
Да ☐ Нет ☐

Страдаете хроническим желудочно-кишечным заболеванием
Да ☐ Нет ☐

Далее нам важно получить информацию о Ваших привычках в еде. При ответе на каждый вопрос отметьте, как часто Вы употребляли продукт, указанный в вопросе, **<u>за последние двенадцать месяцев</u>**.

РЫБА И МОРЕПРОДУКТЫ / ТРАДИЦИОННАЯ ПИЩА

Как часто Вы употребляли рыбу <u>за последние двенадцать месяцев</u>?

	Никогда/ редко	1 в мес.	2-3 в мес.	1 в нед.	2-3 в нед.	4 -6 в нед.	1 в день	2+ в день
Рыба	☐	☐	☐	☐	☐	☐	☐	☐

В период, когда Вы употребляли рыбу, как часто Вы ели нижеприведенные продукты? (Выберите по одному ответу в каждой строке)

	Никогда/ редко	1 в мес.	2-3 в мес.	1 в нед.	2 в нед.	3+ в нед.
Вареная, припущенная треска, пикша, сайда	☐	☐	☐	☐	☐	☐
Жареная треска, пикша, сайда	☐	☐	☐	☐	☐	☐
Зубатка, камбала, морской окунь	☐	☐	☐	☐	☐	☐
Лосось (сёмга), форель	☐	☐	☐	☐	☐	☐
Скумбрия	☐	☐	☐	☐	☐	☐
Сельдь	☐	☐	☐	☐	☐	☐
Горбуша	☐	☐	☐	☐	☐	☐
Сиг, чир, пелядь, ряпушка, голец, омуль, нельма и др. подобная рыба	☐	☐	☐	☐	☐	☐

Если Вы употребляли <u>другую рыбу</u>, впишите в пустые графы ниже название рыбы и укажите, как часто Вы её употребляли

	Никогда/ редко	1 в мес.	2-3 в мес.	1 в нед.	2 в нед.	3+ в нед.
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐

Опишите, какую рыбу Вы едите чаще, начиная с наиболее часто потребляемой рыбы 1 и заканчивая наименее часто потребляемой 3.

1 наиболее часто	
2	
3 наименее часто	

Зависит ли значительно Ваше потребление рыбы от сезона года?

Да ☐ Нет ☐ Не знаю ☐

Если Да, укажите, <u>преимущественно</u>, какую рыбу в какое время года и как часто (выберите *1 в мес.; 2-3 в мес.; 1 в нед.; 2 в нед.; 3+ в нед.*) Вы употребляете.

Сезон	Виды потребляемой рыбы	Как часто
зима		
весна		
лето		
осень		

Если Вы ели рыбу, сколько составляла обычная порция? (1 порция =150 г) (Выберите по одному ответу в каждой строке)

Вареная, припущенная рыба (порция)

☐1 ☐1.5 ☐2 ☐3+

Жареная рыба (порция)

☐1 ☐1.5 ☐2 ☐3+

<u>Сколько раз в год</u> Вы ели следующие продукты? (Выберите по одному ответу в каждой строке)

	0	1-3	4-6	7-9	10+
Молоки	☐	☐	☐	☐	☐
Печень рыбы	☐	☐	☐	☐	☐

Как часто Вы употребляли консервы печень трески? _____ раз в месяц. **Отметьте 0, если реже.**

Как часто Вы ели морских ракообразных (креветки, крабы)? (Выберите только один вариант ответа)

☐никогда/редко ☐1 в мес. ☐2-3 в мес. ☐1+ в нед.

Как часто Вы ели морских моллюсков (мидии, кальмары, морские гребешки)? (Выберите только один вариант ответа)

☐никогда/редко ☐1 в мес. ☐2-3 в мес. ☐1+ в нед.

По Вашим оценкам, достаточно ли рыбы Вы потребляли?

Да ☐ Нет ☐

Если Нет, почему Вы не потребляли больше рыбы?

	Да	Нет
Слишком дорого	☐	☐
Маленький выбор	☐	☐
Трудно купить свежую рыбу	☐	☐
Плохое качество	☐	☐
Отсутствуют блюда быстрого приготовления	☐	☐
Запах во время приготовления	☐	☐
Трудно приготовить	☐	☐
Не люблю вкус	☐	☐
Члены семьи не любят рыбу	☐	☐
Семейная привычка, мы не ели рыбу в моём детстве	☐	☐
Пищевая аллергия	☐	☐

Если другое важно, пожалуйста, укажите подробную информацию

.....

.....

Как Вы считаете, изменилась ли доступность рыбы с 1991 года?

☐Меньше доступна ☐Больше доступна ☐Не изменилась

Как часто Вы или члены Вашей семьи ловили рыбу?

Еженедельно ☐

1-3 раза в месяц ☐

1-11 раз в год ☐

Никогда ☐

Какую часть от всех продуктов питания, потребляемых Вашей семьей, составляла рыба?

Ничего/почти ничего ☐ Больше половины ☐

Меньше половины ☐ Почти всё ☐

Около половины ☐ Не знаю ☐

Какую часть от всей рыбы, потребляемой Вашей семьей, составляла заготовленная Вами рыба?

Ничего/почти ничего ☐ Больше половины ☐

Меньше половины ☐ Почти всё ☐

Около половины ☐ Не знаю ☐

Как часто Вы ели следующие виды традиционной северной пищи? (Выберите по одному ответу в каждой строке)

	Никогда/ редко	1 раз в мес.	2-3 раза в мес.	1 раз в нед.	2-3 раза в нед.	4+ раз в нед.
Оленье мясо	☐	☐	☐	☐	☐	☐
Олений жир	☐	☐	☐	☐	☐	☐
Мясо диких животных	☐	☐	☐	☐	☐	☐
Мясо тюленя	☐	☐	☐	☐	☐	☐
Жир тюленя	☐	☐	☐	☐	☐	☐
Мясо моржа	☐	☐	☐	☐	☐	☐
Жир моржа	☐	☐	☐	☐	☐	☐
Мясо кита	☐	☐	☐	☐	☐	☐
Китовый жир	☐	☐	☐	☐	☐	☐
Северные лесные ягоды	☐	☐	☐	☐	☐	☐
Северные лесные грибы	☐	☐	☐	☐	☐	☐
		Другое				
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐

Вспомните, какая часть Вашего меню состояла из традиционных северных продуктов питания, включая рыбу?

Ничего/почти ничего ☐ Больше половины ☐

Меньше половины ☐ Почти всё ☐

Около половины ☐ Не знаю ☐

Из общего объема традиционной северной пищи, потребляемой в Вашей семье, какая часть была добыта членами Вашей семьи в последние 12 месяцев путем охоты, рыбалки, собирательства?

Ничего/ почти ничего ☐ Больше половины ☐

Меньше половины ☐ Почти всё ☐

Около половины ☐ Не знаю ☐

ДРУГИЕ ПРОДУКТЫ И ПРИГОТОВЛЕНИЕ ПИЩИ

При ответе на каждый вопрос отметьте, как часто Вы употребляли продукт, указанный в вопросе, **за последние двенадцать месяцев**.

Сколько стаканов каждого вида молока (кисломолочных продуктов) Вы пили? (Выберите по одному ответу в каждой строке):

	Никогда/ редко	1-4 ст. в нед.	5-6 ст. в нед.	1 ст. в день	2-3 ст. в день	4+ ст. в день
Молоко (кисломолочные продукты) жирностью 3,2-3,9%	☐	☐	☐	☐	☐	☐
Молоко (кисломолочные продукты) жирностью 1,5-2,5%	☐	☐	☐	☐	☐	☐
Обезжиренное молоко 0,5%	☐	☐	☐	☐	☐	☐

Употребляли ли Вы сливки 10% и >?

Да, практически ежедневно ☐ Иногда ☐ Нет ☐

Сколько чашек чая, каждого вида кофе Вы пили? (Выберите по одному ответу в каждой строке)

	Никогда/ редко	1-6 ч. в нед.	1 ч. в день	2-3 ч. в день	4-5 ч. в день	6-7 ч. в день	8+ ч. в день
Чай	☐	☐	☐	☐	☐	☐	☐
Сваренный кофе	☐	☐	☐	☐	☐	☐	☐
Приготовленный фильтрационным способом или быстрорастворимый кофе	☐	☐	☐	☐	☐	☐	☐

Сколько стаканов пакетированных соков или газированных напитков, содержащих сахар, Вы пили? (Выберите только один вариант ответа)

	Никогда/ редко	1-3 ст. в нед.	4-6 ст. в нед.	1 ст. в день	2-3 ст. в день	4+ ст. в день
Пакетированные соки, газированные напитки, содержащие сахар	☐	☐	☐	☐	☐	☐

Сколько примерно кусков или чайных ложек рафинированного сахара Вы обычно клали в напитки (чай, кофе и другие) в среднем в день? Отметьте 0, если Вы не используете сахар.

_____ кусков или чайных ложек сахара в день

Как часто Вы употребляли следующие продукты? (Выберите по одному ответу в каждой строке)

	Никогда/ редко	1 в мес.	2-3 в мес.	1 раз в нед.	несколько раз в нед.	1 раз в день	2+ раз в день
Творог и творожные изделия	☐	☐	☐	☐	☐	☐	☐
Сметана	☐	☐	☐	☐	☐	☐	☐
Сливочное масло	☐	☐	☐	☐	☐	☐	☐
Маргарин	☐	☐	☐	☐	☐	☐	☐
Йогурт	☐	☐	☐	☐	☐	☐	☐

Как часто в среднем Вы употребляли злаки (сухие продукты из смеси зёрен), овсяные хлопья, мюсли? (Выберите только один вариант ответа)

Никогда/редко	1-3 в нед.	4-6 в нед.	1 в день
☐	☐	☐	☐

Сколько кусков хлебобулочных изделий и сухих хлебцев Вы употребляли (1/2 булочки = 1 кусок хлеба)? (Выберите по одному ответу в каждой строке)

	Никогда/ редко	1-4 в нед.	5-7 в нед.	2-3 в день	4-5 в день	6+ в день
Ржаной (чёрный хлеб)	☐	☐	☐	☐	☐	☐
Хлеб из муки грубого помола,цельнозерновой	☐	☐	☐	☐	☐	☐
Пшеничный хлеб (белый хлеб, батон)	☐	☐	☐	☐	☐	☐
Сухие хлебцы и т.д.	☐	☐	☐	☐	☐	☐

Сколько бутербродов в среднем за неделю Вы употребляли со следующими рыбными продуктами? (Выберите по одному ответу в каждой строке)

	Никогда/ редко	1 в нед.	2-3 в нед.	4-6 в нед.	7-9 в нед.	10+ в нед.
Консервированная рыба	☐	☐	☐	☐	☐	☐
Слабосолёная жирная рыба	☐	☐	☐	☐	☐	☐
Икра	☐	☐	☐	☐	☐	☐

Сколько бутербродов в среднем за неделю Вы употребляли с другими продуктами? (Выберите по одному ответу в каждой строке)

	Никогда/ редко	1-3 в нед.	4-6 в нед.	1 в день	2-3 в день	4+ в день
Варенье, джем, мёд						
Твёрдый сыр жирностью 40-50%	☐	☐	☐	☐	☐	☐
Обезжиренный твёрдый сыр	☐	☐	☐	☐	☐	☐
Плавленый сыр	☐	☐	☐	☐	☐	☐
Мясные продукты (колбаса, ветчина, бекон и др.), печеночный паштет	☐	☐	☐	☐	☐	☐

Какой вид жира Вы обычно использовали с хлебом? (Выберите более чем один вариант, если необходимо)

Я не использую жиры для бутербродов ☐
Сливочное масло ☐
Мягкий маргарин (напр., «Воймикс», «Рама») ☐
Сало и другой жир домашних животных ☐
Другой вид жира (напишите какой): _____

Если Вы использовали жир для бутербродов, каков слой данного продукта? (Выберите только один вариант ответа)

Очень тонкий слой (3 г, меньше чайной ложки) ☐
Тонкий слой (5 г, 1 чайная ложка) ☐
Толстый слой (8 г, 1,5 чайной ложки) ☐
Очень толстый слой (12 г, больше 2 чайных ложек) ☐

Как часто Вы употребляли свиное сало? Отметьте 0, если Вы редко/никогда не едите сало.

_____ раз в неделю

Как часто Вы употребляли майонез? (Выберите только один вариант ответа)

	Никогда/ редко	1-6 в нед.	1 в день	2-3 в день	4+ в день
Майонез	☐	☐	☐	☐	☐

Как часто Вы употребляли рис, спагетти/макароны, бобовые? (Выберите по одному ответу в каждой строке)

	Никогда/ редко	1-3 в мес.	1 в нед.	2 в нед.	3+ в нед.
Рис	☐	☐	☐	☐	☐
Макароны	☐	☐	☐	☐	☐
Бобовые	☐	☐	☐	☐	☐

Как часто Вы употребляли каши (рисовая, гречневая, пшённая, перловая, ячневая, манная, овсяная)? (Выберите только один вариант ответа)

	Никогда/ редко	1 в мес.	2-3 в мес.	1 в нед.	2 в нед.	3+ в нед.
Каши	☐	☐	☐	☐	☐	☐

Как часто Вы употребляли орехи, семечки? (Выберите по одному ответу в каждой строке)

	Никогда/ редко	1-3 в мес.	1 в нед.	2-4 в нед.	5-6 в нед.	1 в день	2+ в день
Орехи	☐	☐	☐	☐	☐	☐	☐
Семечки	☐	☐	☐	☐	☐	☐	☐

Как часто Вы употребляли фрукты: яблоки/груши, апельсины, бананы, виноград, персики и др.? (Выберите только один вариант ответа)

	Никогда/ редко	1-3 в мес.	1 в нед.	2-4 в нед.	5-6 в нед.	1 в день	2+ в день
Фрукты	☐	☐	☐	☐	☐	☐	☐

Как часто Вы употребляли овощи, исключая картофель? (Выберите только один вариант ответа)

	Никогда/ редко	1-3 в мес.	1 в нед.	2 в нед.	3 в нед.	4-5 в нед.	6-7 в нед.
Овощи	☐	☐	☐	☐	☐	☐	☐

Как часто Вы употребляли картофель? (Выберите по одному ответу в каждой строке)

	Никогда/ редко	1-3 в мес.	1 в нед.	2-3 в нед.	4-6 в нед.	7+ в нед.
Вареный картофель	☐	☐	☐	☐	☐	☐
Жареный картофель	☐	☐	☐	☐	☐	☐

Какой жир Вы обычно использовали при приготовлении пищи? (Вы можете выбрать более одного ответа)

- Подсолнечное масло ☐
- Сливочное масло ☐
- Твердый маргарин ☐
- Мягкий маргарин ☐
- Сливочное масло с добавками маргарина ☐
- Соевое масло ☐
- Оливковое масло ☐
- Кукурузное масло ☐
- Животный жир (свиное сало, говяжий, куриный и др.) ☐
- Другой, напишите какой именно: ☐
- Ничего ☐

Чем Вы обычно заправляли салаты? (Вы можете выбрать более одного ответа)

- Подсолнечное масло ☐
- Майонез ☐
- Сметана ☐
- Оливковое масло ☐
- Соевое масло ☐
- Кукурузное масло ☐
- Другое, напишите что именно ☐
- Ничего ☐

Сколько яиц Вы обычно съедали за неделю (в жареном, вареном виде, в омлете)? (Выберите только один вариант ответа)

☐0 ☐1 ☐2 ☐3-4 ☐5-6 ☐7+

Как часто Вы употребляли?

	Никогда/ редко	1-3 в мес.	1 в нед.	2-3 в нед.	4-6 в нед.	7+ в нед.
Выпечку, мучные кондитерские изделия	☐	☐	☐	☐	☐	☐
Конфеты, шоколад	☐	☐	☐	☐	☐	☐

Какие основные блюда Вы ели на обед, ужин. Укажите, как часто в среднем Вы употребляли то или иное блюдо за последние двенадцать месяцев. (Выберите по одному ответу в каждой строке)

	очень редко	1 в мес.	2-3в мес.	1 в нед.	2 в нед.	3 в нед.	4 в нед.	5+ в нед.
Порция мяса (говядина, свинина, баранина)	☐	☐	☐	☐	☐	☐	☐	☐
Фарш, котлета мясная (говядина, свинина, баранина)	☐	☐	☐	☐	☐	☐	☐	☐
Переработанное мясо: сосиски и т.д.	☐	☐	☐	☐	☐	☐	☐	☐
Консервированное мясо («Тушёнка»)	☐	☐	☐	☐	☐	☐	☐	☐
Субпродукты, напр. печень (говядина, свинина, баранина)	☐	☐	☐	☐	☐	☐	☐	☐
Курица, блюда из птицы	☐	☐	☐	☐	☐	☐	☐	☐
Порция жирной рыбы (скумбрия, лосось и т.д.)	☐	☐	☐	☐	☐	☐	☐	☐
Порция постной рыбы (треска и т.д.)	☐	☐	☐	☐	☐	☐	☐	☐
Натуральный мясной, куриный бульон (суп на их основе)	☐	☐	☐	☐	☐	☐	☐	☐
Уха, рыб. бульон	☐	☐	☐	☐	☐	☐	☐	☐
Другое								
	☐	☐	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐	☐	☐

Как часто Вы ели солёные закуски, «фаст-фуд»? (Выберите по одному ответу в каждой строке)

	Никогда/ редко	1-3 в мес.	1 в нед.	2-3 в нед.	4-6 в нед.	7+ в нед.
Картофельные чипсы	☐	☐	☐	☐	☐	☐
Арахис	☐	☐	☐	☐	☐	☐
Сушёную рыбу, кальмары	☐	☐	☐	☐	☐	☐
«Фаст-фуд» (картошка фри, пицца, гамбургер)	☐	☐	☐	☐	☐	☐

Как часто Вы употребляли мороженые полуфабрикаты?

☐никогда/редко ☐1-3 в мес. ☐1 в нед.
☐2-3 в нед. ☐4-6 в нед. ☐7+ в нед.

Как часто Вы жарили пищу?

Никогда/ редко	Иногда, не каждый день	Каждый день
☐	☐	☐

Как часто вы ели курицу вместе с кожей?

- Всегда ☐
- Часто ☐
- Иногда ☐
- Никогда ☐
- Я не ем курицу ☐

Добавляете ли Вы соль в уже приготовленную пищу?

Нет, никогда ☐ Да, обычно ☐ Да, иногда ☐

Удаляете ли Вы видимый жир с мяса до его приготовления или перед употреблением в пищу?

Да ☐ Нет ☐

Сколько раз в день Вы принимаете пищу?_____Раз

Пищевые добавки

Принимаете ли Вы рыбий жир жидкий?

Да ☐↓ Нет ☐

Напишите название	Никогда/ редко	1-3 в месяц	1 в нед.	2-3 нед.	4-6 нед.	7 нед.	Как долго
	☐	☐	☐	☐	☐	☐	_ _ лет _ _ месяцев

Принимаете ли Вы рыбий жир (омега-3 добавки) в капсулах?

Да ☐ ↓ Нет ☐

Напишите название	Никогда/ редко	1-3 в месяц	1 в нед.	2-3 нед.	4-6 нед.	7 нед.	Как долго
	☐	☐	☐	☐	☐	☐	_ _ лет _ _ месяцев

Принимаете ли Вы витамины/минералы?

Да ☐↓ Нет ☐

Напишите название	Никогда/ редко	1-3 в месяц	1 в нед.	2-3 нед.	4-6 нед.	7 нед.	Как долго
1	☐	☐	☐	☐	☐	☐	_ _ лет _ _ месяцев
2	☐	☐	☐	☐	☐	☐	_ _ лет _ _ месяцев
3	☐	☐	☐	☐	☐	☐	_ _ лет _ _ месяцев

Принимаете ли Вы другие пищевые добавки?

Да ☐↓ Нет ☐

Напишите название	Никогда/ редко	1-3 в месяц	1 в нед.	2-3 нед.	4-6 нед.	7 нед.	Как долго
1	☐	☐	☐	☐	☐	☐	_ _ лет _ _ месяцев
2	☐	☐	☐	☐	☐	☐	_ _ лет _ _ месяцев
3	☐	☐	☐	☐	☐	☐	_ _ лет _ _ месяцев

Семейный анамнез

Укажите, был(а) ли у кого-либо из Ваших близких родственников (родители, родные сёстры, братья) в возрасте до 60 лет:

	Да	Нет	Не знаю
Инфаркт миокарда или острый сердечный приступ	☐	☐	☐
Инсульт, кровоизлияние в мозг	☐	☐	☐
Гипертония	☐	☐	☐
Внезапная сердечная смерть	☐	☐	☐

Укажите, страдал ли кто-либо из Ваших близких родственников (родители, родные сёстры, братья) сахарным диабетом?

Да ☐ Нет ☐ Не знаю ☐

Укажите, у кого-либо из Ваших близких родственников (родители, родные сёстры, братья) есть (были)

проблемы с контролем избыточного веса?

Да ☐ Нет ☐ Не знаю ☐

повышенный уровень холестерина?

Да ☐ Нет ☐ Не знаю ☐

Здоровье

Есть ли у Вас какие-нибудь хронические заболевания или проблемы со здоровьем?

Да ☐ Нет ☐ Не знаю, нет ответа ☐

Если «Да», укажите, пожалуйста, какие у Вас есть хронические заболевания или проблемы со здоровьем (в т.ч. гинекологические)?

.....

.....

.....

.....

.....

.....

Есть ли у Вас какие-либо жалобы на состояние здоровья в настоящее время?

Да ☐ Нет ☐

Было ли у Вас острое респираторное заболевание (ОРЗ) или обострение хронического заболевания в течение последних 2-3 недель?

Да ☐ Нет ☐ Не знаю, нет ответа ☐

В последний месяц (30 дней) были ли у Вас какие-либо из перечисленных ниже симптомов или жалоб?

	Да	Нет
Боли в груди во время физической нагрузки	☐	☐
Проблемы дыхания или кашель	☐	☐
Боли в шее, плече	☐	☐
Головные боли	☐	☐
Отёки на ногах	☐	☐
Приступы головокружения	☐	☐
Боли в суставах	☐	☐
Боли в спине	☐	☐
Проблемы пищеварения	☐	☐
Высокая температура	☐	☐
Болезни, выпадение зубов	☐	☐
Болезни или раздражение кожи	☐	☐
Нарушение зрения	☐	☐
Нарушение слуха	☐	☐
Проблемы со сном, бессонница	☐	☐

Когда-либо доктор, медицинская сестра или другой медицинский работник говорили Вам, что у Вас есть какие-либо из перечисленных ниже заболеваний? В каком возрасте Вам впервые об этом сказали? Получали ли Вы какое-либо лечение или принимали ли лекарства от этого состояния последние 12 месяцев?

Высокое артериальное давление, гипертония

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Было ли высоким артериальное давление во время беременности?

Да ☐ Нет ☐ Давление на верхней границе нормы (пре-гипертензия)☐

Сердечная недостаточность

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Сердечный приступ, инфаркт миокарда

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Флебит (воспаление вен/артерий)

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Тромбоз верхних или нижних конечностей

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Инсульт

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Стенокардия, ишемическая болезнь сердца

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Аритмия

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Мигрень, частая головная боль

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Бронхиальная астма

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Другие аллергические заболевания

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Если Да, какие .....

Рак. Тип? .....

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Диабет. Тип? .....

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Был ли сахар высоким во время беременности?
Да ☐ Нет ☐Сахар на верхней границе нормы (пре-диабет)☐

Заболевания желчного пузыря (камни в желчном пузыре, застой желчи, воспаление желчного пузыря)

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Болезни печени (гепатит, цирроз, печёночная недостаточность)

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Заболевания почек (гломерулонефрит, пиелонефрит, мочекаменная болезнь, почечная недостаточность)

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Заболевания щитовидной железы

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Хроническая тревога, хроническая депрессия

Наличие заболевания: Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Была ли у Вас аллергия на определенные виды продуктов?

Да ☐ Нет ☐

Если Да, отметьте на какие:

Молоко и т.д. ..... ☐

Цитрусовые (апельсины и т.д.) ..... ☐

Рыба ..... ☐

Ракообразные ..... ☐

Другие (какие) .....

Как бы Вы сказали о своём здоровье, что оно?

Отличное ..... ☐

Очень хорошее ..... ☐

Хорошее ..... ☐

Удовлетворительное ..... ☐

Плохое ..... ☐

Не знаю ..... ☐

Говорил ли Вам врач или медицинская сестра, что у Вас избыточный вес, ожирение?
Да☐ Нет ☐ Нет ответа☐

В каком возрасте Вам впервые сказали? ..... Нет ответа☐

Получали ли Вы какое-либо лечение или лекарства от этого состояния последние 12 месяцев? Да☐ Нет ☐

Говорил ли Вам врач или медицинская сестра, что у Вас высокий уровень холестерина?
Да ☐ Нет ☐ Не знаю☐

Когда Вам делали анализ крови на холестерин последний раз?
В течение предыдущего года..... ☐
1-5 лет назад..... ☐
Более чем 5 лет назад..... ☐
Никогда..... ☐
Не знаю ..... ☐

Последний раз Ваш холестерин был.....

Давали ли Вам медицинские работники рекомендации изменить Ваше питание из-за здоровья?
Да ☐ Нет ☐ Не знаю☐

Менструации

В каком возрасте у Вас была первая менструация?

В I _ I _ I лет

Через какой период Ваш менструальный цикл стал регулярным?
Через 1 год или менее ☐ Более, чем через год☐
До сих пор нерегулярный ☐ Не помню☐

До сих пор ли Ваш менструальный цикл регулярный?
Да ☐ Нет менструаций ☐
Мой менструальный цикл нерегулярный ☐

Если нет:
Закончился ли по физиологической причине? ☐
Были ли удалены фаллопиевы трубы (придатки)? ☐
Была ли удалена матка (гистерэктомия)? ☐
Закончился ли менструальный цикл по другой причине? ☐

Вы беременны?
Да ☐ Нет ☐

В каком возрасте у Вас полностью прекратились менструации?

В I _ I _ I лет

Как долго у Вас нет менструаций (с последней менструации)?
Меньше, чем 1 год ☐
1-5 лет ☐
5-10 лет ☐
Больше, чем 10 лет ☐

Беременности, роды, грудное вскармливание

Укажите год рождения и количество месяцев грудного вскармливания каждого ребенка (пожалуйста, сообщите о мертворожденных детях или умерших после родов). Если у Вас нет, и не было детей, переходите к следующему вопросу.

Ребёнок	Год рождения	Количество месяцев грудного вскармливания
1	☐☐☐☐	☐☐
2	☐☐☐☐	☐☐
3	☐☐☐☐	☐☐
4	☐☐☐☐	☐☐
5	☐☐☐☐	☐☐
6	☐☐☐☐	☐☐
7	☐☐☐☐	☐☐
8	☐☐☐☐	☐☐

Гормональная контрацепция

КОНТРАЦЕПТИВНЫЕ ТАБЛЕТКИ

Употребляли ли Вы когда-либо контрацептивные таблетки?
Да ☐ Нет ☐

Если Да, как долго Вы употребляли контрацептивные таблетки?

I _ I _ I лет

В каком возрасте Вы начали употреблять контрацептивные таблетки?

BI _ I _ I лет

Употребляете ли Вы сейчас контрацептивные таблетки?
Да ☐ Нет ☐

Если Да, напишите название препарата.....

Употребление гормональных препаратов в период менопаузы

ЭСТРОГЕНСОДЕРЖАЩИЕ ГОРМОНАЛЬНЫЕ ТАБЛЕТКИ/ПЛАСТЫРИ/КРЕМА/СУППОЗИТОРИИ

Употребляли ли Вы когда-либо гормональные таблетки/пластыри?
Да ☐ Нет ☐

Если Да, как долго Вы употребляли гормональные таблетки/пластыри?

I _ I _ I лет

В каком возрасте Вы начали употреблять гормональные таблетки/пластыри?

BI _ I _ I лет

Употребляете ли Вы сейчас таблетки/пластыри?
Да ☐ Нет ☐

Если Да, напишите название препарата.....

ГОРМОНАЛЬНЫЕ ПРЕПАРАТЫ ДЛЯ ВАГИНАЛЬНОГО ИСПОЛЬЗОВАНИЯ

Употребляли ли Вы когда-либо гормональные крема/суппозитории?
Да ☐ Нет ☐

Если Да, как долго Вы употребляли гормональные крема/суппозитории?
I _ I _ I лет

В каком возрасте Вы начали употреблять гормональные крема/суппозитории?
BI _ I _ I лет

Употребляете ли Вы сейчас крема/суппозитории?
Да ☐ Нет ☐

Если Да, напишите название препарата.....

Использование лекарств

Препараты для сердечно-сосудистой системы

Принимали ли Вы препараты *регулярно*?

	Да	Нет
От высокого давления?	☐	☐
От стенокардии?	☐	☐
От сердечной недостаточности и/или при неправильном сердцебиении	☐	☐

Если Вы ответили Да на один или более вышеуказанных вопросов, пожалуйста, укажите, какие препараты для сердечно-сосудистой системы Вы используете и когда начали лечение.

Препарат	Начало лечения Год / Месяц
1.....	
2.....	
3.....	
4.....	
5.....	

Принимаете ли Вы регулярно таблетки, содержащие ацетилсалициловую кислоту (аспирин) для профилактики сердечных заболеваний?
Да ☐ Сейчас нет, но принимал(а) раньше ☐
Нет, никогда не принимал(а) ☐

Если Да, укажите название.....
Как долго Вы употребляете их..... месяцев ..... лет

Принимаете ли Вы *регулярно* препараты, понижающие уровень холестерина?
Да ☐ Сейчас нет, но принимал(а) раньше ☐
Нет, никогда не принимал(а) ☐

Если Да, укажите название.....
Как долго Вы употребляете их..... месяцев ..... лет

Принимали ли Вы какие-либо препараты на протяжении последних двух недель?
Да ☐ Нет ☐

Если Да, это были лекарства: (выберите Да/Нет по каждому пункту)

Лекарства		Да	Нет
От высокого давления		☐	☐
Другие сердечные препараты		☐	☐
Для снижения холестерина		☐	☐
От диабета:	Таблетки	☐	☐
	Инсулин	☐	☐
От боли		☐	☐
От астмы		☐	☐
От симптомов аллергии		☐	☐
От хронического бронхита или эмфиземы		☐	☐
От депрессии		☐	☐
От нарушений пищеварения		☐	☐
От бессонницы		☐	☐
Успокоительные		☐	☐
От простуды, гриппа, болей в горле		☐	☐
Противовоспалительные гормоны (такие как преднизолон)		☐	☐
Витамины/минералы		☐	☐
Другие:		☐	☐

Вес

Телосложение в начальной школе. (Выберите только один вариант ответа)
Очень худощавая/ый☐ Худощавая/ый☐ Нормальная/ый☐
Полная/ый☐ Очень полная/ый☐

Телосложение в возрасте 18 лет. (Выберите только один вариант ответа)
Очень худощавая/ый☐ Худощавая/ый☐ Нормальная/ый☐
Полная/ый☐ Очень полная/ый☐

Пытаетесь ли Вы изменить Ваш вес?
☐Нет
☐Да, я пытаюсь набрать вес ☐Да, я пытаюсь снизить вес

Физическая активность

Пожалуйста, укажите уровень Вашей физической активности по шкале от самого низкого до самого высокого уровня в возрасте от 14 до 30 лет, а также на сегодняшний день. Ниже представлена шкала от 1 до 10. Под физической активностью мы понимаем физическую нагрузку на улице и дома, а также тренировки/физические упражнения и другие виды физической активности, напр., прогулки и т.д. Обведите число, наиболее точно характеризующее уровень Вашей физической активности.

Возраст	Очень низкий									Очень высокий
14 лет	1	2	3	4	5	6	7	8	9	10
30 лет	1	2	3	4	5	6	7	8	9	10
Сейчас	1	2	3	4	5	6	7	8	9	10

Тренировались ли Вы / делали ли физические упражнения для здоровья (не менее 30 минут) регулярно последние 12 месяцев?
Да ☐ Нет ☐

Если Да, то:

сколько месяцев..... месяцев

сколько часов в неделю..... часов

Сколько минут или часов в день в среднем Вы ходите / гуляете на открытом воздухе, в том числе до места Вашей работы и обратно?

	Редко/никогда	Меньше 30 минут	30 минут-1час	1-2 часа	Больше 2 часов
Зима	☐	☐	☐	☐	☐
Весна	☐	☐	☐	☐	☐
Лето	☐	☐	☐	☐	☐
Осень	☐	☐	☐	☐	☐

Какова степень физической нагрузки на Вашей работе?

В основном сижу. Во время работы я хожу мало. Пример: офисная работа за столом.	☐
В основном хожу. Я хожу много, но мне не приходится поднимать и переносить тяжести. Пример: продавец, офисная работа, требующая много ходьбы.	☐
Поднимаю и переношу небольшие тяжести. На работе мне приходится много ходить и носить тяжести или часто подниматься по лестнице или в гору. Пример: почтальон, строитель.	☐
Занимаюсь тяжёлой физической работой. Физически моя работа очень тяжёлая, мне приходится поднимать и носить тяжести, копать. Пример: тяжёлая сельскохозяйственная работа или промышленная работа.	☐
Я не работаю	☐

В свободное от работы время как часто Вы выполняете физические упражнения, другую физическую нагрузку (работа по дому или на даче, быстрая ходьба) продолжительностью не менее 30 минут, такую, чтобы появилась небольшая одышка или выступил пот?

Ежедневно	☐
4-6 раз в неделю	☐
2-3 раза в неделю	☐
Один раз в неделю	☐
2-3 раза в месяц	☐
Несколько раз в год и меньше	☐
Я не могу из-за болезни, инвалидности	☐

Какова степень Вашей физической активности в свободное от работы время? Если это зависит от сезона, отметьте группу, которая отражает степень физической активности в среднем за год. (Выберите один вариант ответа)

Я в основном читаю, смотрю телевизор и делаю то, что не требует физической активности (в основном, сидячий образ жизни в свободное время).	☐
Я хожу, катаюсь на велосипеде или двигаюсь другим образом не менее 4-х часов в неделю (это включает прогулки, лёгкую работу на огороде, ходьбу на работу и с работы).	☐
Физическая активность включает занятия спортом на любительском уровне для поддержания здоровья и физической формы, т.е. занятия бегом, лыжами, гимнастикой, плаванием, играми с мячом, выполнение достаточно тяжёлой работы на огороде или равнозначные этому виды деятельности не менее 4-х часов в неделю.	☐
В моё свободное время я занимаюсь спортом профессионально, регулярно, несколько дней в неделю, участвую в соревнованиях по бегу, играм с мячом и в других видах спорта, требующих тяжёлой физической нагрузки.	☐

Сколько обычно времени в будний день, в свободное от работы время, Вы проводите сидя (сидя за столом, в гостях у друзей, за чтением, в транспорте, смотрите телевизор, лёжа или сидя)?

.....часов.....минут

Алкоголь

Употребляете ли Вы алкоголь?

Да ☐ Нет ☐

Если да, как часто и какое количество Вы в среднем выпивали за 12 месяцев? (Выберите по одному ответу в каждой строке)

	Никогда/редко	1 в мес.	2-3 в мес.	1 в нед.	2-4 в нед.	5-6 в нед.	1+ в ден.
Лёгкое пиво (5%, бутылок 1/2 литра)	☐	☐	☐	☐	☐	☐	☐
Крепкое пиво (более 5%, бутылок 1/2 литра)	☐	☐	☐	☐	☐	☐	☐
Столовое вино, шампанское (менее 12%, бокалов 120 мл)	☐	☐	☐	☐	☐	☐	☐
Креплёное вино, наливки (16-20%, бокалов 80 мл)	☐	☐	☐	☐	☐	☐	☐
Крепкие спиртные напитки: водка, коньяк, самогон, в том числе в коктейлях (40%, рюмок 40 мл)	☐	☐	☐	☐	☐	☐	☐

Сколько лет Вы употребляете алкоголь в таких количествах? I _ I _ I лет

Вспомните, сколько бокалов, бутылок следующего алкоголя Вы выпили за последние 7 дней? Если Вы не пили, отметьте 0. (Выберите по одному ответу в каждой строке)

Лёгкое пиво (крепостью менее 5%, бутылок 1/2 литра)	
Крепкое пиво (крепостью более 5%, бутылок 1/2 литра)	
Столовое вино, шампанское (крепостью менее 12%,бокалов 120 мл)	
Креплёное вино, наливки (крепостью 16-20%, бокалов 80 мл)	
Крепкие спиртные напитки: водка, коньяк, самогон, в том числе в коктейлях (крепостью 40%, рюмок 40 мл)	

Не возникает ли у Вас мысль о необходимости отказаться от употребления алкоголя?

Да ☐ Нет ☐

Не надоедает ли Вам критика окружающих по поводу Ваших выпивок?

Да ☐ Нет ☐

Не возникает ли у Вас переживаний или чувства вины в связи с Вашими выпивками?

Да ☐ Нет ☐

Не бывает ли так, что Вы по утрам в первую очередь принимаетесь за выпивку для успокоения нервов или устранения явлений похмелья?

Да ☐ Нет ☐

Курение

Проживаете (проживали) ли Вы с заядлым курильщиком

в настоящее время? Да ☐ Нет ☐

в детстве? Да ☐ Нет ☐

Сколько часов в среднем в день Вы находитесь в накуренном помещении?

Больше, чем 5 часов ☐ 1-5 часов ☐

Меньше, чем 1 час в день ☐ Почти нисколько ☐

Вы курите в настоящее время?

- Да, каждый день ☐
- Да, иногда, не каждый день ☐
- Нет, я никогда не курил(а) или я выкурил(а) не более 100 сигарет (примерно 5 пачек) за свою жизнь ☐
- Нет, я курил(а) в прошлом ☐

Что Вы курите (курили): сигареты, папиросы, трубку, самокрутки, сигары? (Обведите в круг)

Укажите в графе «Возраст» количество выкуриваемых в среднем сигарет в день.

Возраст	Количество выкуриваемых сигарет в день						
	0	1-4	5-9	10-14	15-19	20-24	25+
15-19	☐	☐	☐	☐	☐	☐	☐
20-29	☐	☐	☐	☐	☐	☐	☐
30-39	☐	☐	☐	☐	☐	☐	☐
40-49	☐	☐	☐	☐	☐	☐	☐
50-59	☐	☐	☐	☐	☐	☐	☐
60-69	☐	☐	☐	☐	☐	☐	☐

Сколько в целом лет Вы курите (курили) ежедневно? Если меньше, чем 12 месяцев, укажите 00.

| _ | _ | Лет

Сколько в среднем сигарет/папирос Вы курите (курили) ежедневно?

Количество сигарет в день | _ | _ |

В каком возрасте Вы начали курить ежедневно?

Возраст | _ | _ |

Вопрос для тех респондентов, кто бросил курить. Когда Вы бросили курить?

| _ | _ | лет назад

Если последние 12 месяцев:

Меньше чем 1 месяц назад ☐ 1-6 месяцев назад ☐
6-12 месяцев назад ☐

Психологическое здоровье, стресс

Оцените уровень стресса за последний год?

Высокий ☐ Средний ☐ Низкий ☐

Чувствовали ли Вы депрессию за последний год?

- Совсем нет ☐
- Не больше, чем до этого ☐
- Немного больше, чем до этого ☐
- Намного больше, чем до этого ☐
- Не знаю, нет ответа ☐

Чувствовали ли Вы напряжение, испытывали стресс или подвергались давлению за последний месяц (30 дней)?

- Совсем нет ☐
- Да – в некоторой степени, но не больше, чем люди обычно испытывают ☐
- Да – больше, чем люди обычно испытывают ☐
- Да – моя жизнь практически невыносима ☐
- Не знаю, нет ответа ☐

Пожалуйста, скажите, насколько Вы удовлетворены качеством Вашей жизни в целом?

- Очень доволен(а) ☐
- Скорее доволен(а) ☐
- Более или менее ☐
- Скорее не доволен(а) ☐
- Очень не доволен(а) ☐
- Не знаю, нет ответа ☐

Медицинский работник .....

Интервьюер .....

Большое спасибо за участие!

Лабораторные данные

APPENDIX III

Basis for Paper III

Questionnaires

2007
KONFIDENSIELT

MILJØGIFTER I SVANGERSKAPET OG I AMMEPERIODEN

ID-nr:

Universitetet i Tromsø

Romssa universitehta

Universitetet i Tromsø Romssa universitehta

MILJØGIFTER I SVANGERSKAPET OG I AMMEPERIODEN

Vi ber deg fylle ut spørreskjemaet så nøye som mulig.

Skjemaet skal leses optisk. Vennligst bruk blå eller sort penn. Du kan ikke bruke komma, forhøy 0,5 til 1. Bruk blokkbokstaver.

Dersom du får for liten plass på enkelte spørsmål, vennligst noter på siste side, eller ta i bruk et ekstra ark.

Venligst besvar skjema innen en uke etter oppstart i prosjektet. Sendes sammen med blodtrykkssjema til UiT i vedlagte returkonvolutt.

Dato for utfylling av spørreskjema: dag mnd år

Dato .....

SOSIALE FORHOLD

Hva er ditt postnummer? .....

Hva er ditt fødselsår: .....

Hvor mange års skolegang/utdanning har du i alt, ta også med grunnskole og videregående? Antall år

Hvor mange personer er det i ditt hushold? Voksne Barn

Hvor høy er den samlede bruttoinntekten i ditt hushold?

- ☐ Under 150 000 kr
- ☐ 150 000-300 000 kr
- ☐ 301 000-450 000 kr
- ☐ 451 000-600 000 kr
- ☐ 601 000-750 000 kr
- ☐ 751 000-900 000 kr
- ☐ Over 900 000 kr

Hva er ditt yrke?

.....

(Ikke skriv her →)

Beskriv kort din arbeidsplass og arbeidsoppgaver så nøyaktig som mulig:
(Eksempel: skole/undervisning, sykehus/ pasientarbeid/cellegift, butikk/ klær, renseri/renser klær, kontor/dataarbeid, frisør/kunder)

.....

(Ikke skriv her →)

Hva er din arbeidssituasjon? (Sett om nødvendig flere kryss)

- ☐ Arbeider heltid
- ☐ Arbeider deltid
- ☐ Hjemmeværende
- ☐ Under utdanning
- ☐ Arbeidssøkende
- ☐ Under attføring
- ☐ Uføretrygdet

Er du sykemeldt? (Sett ett kryss i hver kolonne)

- ☐ Nei
- ☐ Delvis sykemeldt
- ☐ Fullt sykemeldt

Hvordan er du sykemeldt?

- ☐ Sykemeldt korttids
- ☐ Sykemeldt langtids

OPPVEKST

Hva var din bostedskommune da du ble født, og i hvilke kommuner i Norge har du bodd lengre enn ett år?

Kommune	Fra årstall	Til årstall	*(Ikke skriv her →)*
1 Ved fødsel:			
2			
3			
4			
5			
6			
7			

FAMILIE- OG SPRÅKBAKGRUNN

I Nord-Norge bor det folk med ulik etnisk bakgrunn. Det vil si at de snakker ulike språk og har ulike kulturer. Eksempler på etnisk bakgrunn eller etnisk gruppe er norsk, samisk og kvensk.

Hvilket hjemmespråk har/hadde du, dine foreldre og besteforeldre? (sett ett eller flere kryss)

	Norsk	Samisk	Kvensk	Annet	Vet ikke	Dersom annet beskriv
Morfar	☐	☐	☐	☐	☐	.....
Mormor	☐	☐	☐	☐	☐	.....
Farfar	☐	☐	☐	☐	☐	.....
Farmor	☐	☐	☐	☐	☐	.....
Far	☐	☐	☐	☐	☐	.....
Mor	☐	☐	☐	☐	☐	.....
Jeg selv	☐	☐	☐	☐	☐	.....

Hva er din, din fars og din mors etniske bakgrunn? (sett ett eller flere kryss)

	Norsk	Samisk	Kvensk	Annet	Vet ikke	Dersom annet beskriv
Min bakgrunn	☐	☐	☐	☐	☐	.....
Mors bakgrunn	☐	☐	☐	☐	☐	.....
Fars bakgrunn	☐	☐	☐	☐	☐	.....

Hva regner du deg selv som? (sett ett eller flere kryss)

Norsk ☐ Samisk ☐ Kvensk ☐ Annet ☐ Dersom annet beskriv .....

SVANGERSKAPET

Var dette svangerskapet planlagt?

☐ Ja ☐ Nei

Dersom JA, hvor mange måneder tok det før du ble gravid?

Antall mnd. ☐☐

Trengte du hjelp til å bli gravid i dette svangerskapet?
(Behandlet for barnløshet; hormonstimulering, IVF, mikroinjeksjon ol.)

☐ Ja ☐ Nei

Dersom JA, hva var årsaken?

.....

Hvilken behandling fikk du da?

.....

MORSMELK SOM BABY

Ammet din mor deg da du var baby?

☐ Ja ☐ Nei

Dersom JA, hvor mange måneder til sammen fikk du morsmelk?

Totalt antall mnd. med morsmelk ☐☐ Vet ikke ☐

SELVOPPLEVD HELSE

Oppfatter du din helse som:

☐ Meget god ☐ God ☐ Dårlig ☐ Meget dårlig

VEKT

Hvor mye veide du før svangerskapet? *(I hele kg)*.... ☐☐☐

Hva var din egen fødselsvekt som nyfødt baby?

(Gram) ☐☐☐☐ Vet ikke ☐

Har du noen gang hatt vekttap på 5 kg eller mer, i så fall hvor mange ganger?

☐ Ja ☐ Nei Antall ganger ☐☐

FYSISK AKTIVITET

Vi ber deg angi din fysiske aktivitet etter en skala fra svært liten til svært mye ved 14 års alder, før svangerskapet og i dag. Skalaen nedenfor går fra 1-10. Med fysisk aktivitet mener vi både arbeid i hjemmet og i yrkeslivet samt trening og annen fysisk aktivitet som turgåing ol.

	Svært lite									Svært mye
Alder	1	2	3	4	5	6	7	8	9	10
14 år.....	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Før svangerskapet.....	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
I dag.....	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

RØYK OG ALKOHOL

Beskriv dine røykevaner før og i dette svangerskapet?
(Sett ett kryss)

	Ikke røyker	Av og til	Daglig
6 mnd før svangerskapet.....	☐	☐	☐
Ved svangerskapets start.....	☐	☐	☐
I dag.....	☐	☐	☐

Dersom du røyker eller har røykt, angi antall pr. dag eller pr uke?

	Antall pr dag	Antallpr uke
6 mnd før svangerskapet.....	☐☐	☐☐
Ved svangerskapets start.....	☐☐	☐☐
I dag.....	☐☐	☐☐

Dersom du røyker daglig eller tidligere har røykt daglig, hvor mange år har du da røykt til sammen? Antall år ☐☐

Er du til daglig utsatt for passiv røyking?

☐ Ja ☐ Nei Antall timer daglig ☐☐

Er du totalavholdskvinne?

☐ Ja ☐ Nei

Hvis NEI, hvor ofte og hvor mye har du drukket før dette svangerskapet?
(sett ett kryss for hver linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2-4 pr. uke	5-6 pr. uke	1+ pr. dag
Lettøl/cider *(0,5 l)*.....	☐	☐	☐	☐	☐	☐	☐
Øl/rusbrus *(0,5 l)*.....	☐	☐	☐	☐	☐	☐	☐
Vin *(glass)*.....	☐	☐	☐	☐	☐	☐	☐
Brennevin *(drink/shot)*.....	☐	☐	☐	☐	☐	☐	☐
Likør/Hetvin *(glass)*.....	☐	☐	☐	☐	☐	☐	☐

Dersom NEI, hvor ofte og hvor mye har du drukket i dette svangerskapet?
(sett ett kryss for hver linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2-4 pr. uke	5-6 pr. uke	1+ pr. dag
Lettøl/cider *(0,5 l)*.....	☐	☐	☐	☐	☐	☐	☐
Øl/rusbrus *(0,5 l)*.....	☐	☐	☐	☐	☐	☐	☐
Vin *(glass)*.....	☐	☐	☐	☐	☐	☐	☐
Brennevin *(drink/shot)*.....	☐	☐	☐	☐	☐	☐	☐
Likør/Hetvin *(glass)*.....	☐	☐	☐	☐	☐	☐	☐

TRAN, OMEGA-3 OG FISKEOLJE

Bruker du flytende tran/omega-3/fiskeolje?

☐ Ja ☐ Nei

Hvis JA, hvor ofte tar du flytende tran/omega-3/fiskeolje?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2-6 pr. uke	daglig
Om vinteren.....	☐	☐	☐	☐	☐
Resten av året.....	☐	☐	☐	☐	☐

Hvilken type flytende tran/omega-3/fiskeolje bruker du vanligvis, og hvor mye pleier du å ta hver gang?

	1 ts	½ ss	1+ ss
Navn:	☐	☐	☐
Navn:	☐	☐	☐
Navn:	☐	☐	☐

Bruker du kapsler/piller med tran/omega-3/fiskeolje?

☐ Ja ☐ Nei

Hvis JA, hvor ofte tar du kapsler/piller med tran/omega-3/fiskeolje (Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2-6 pr. uke	daglig
Om vinteren	☐	☐	☐	☐	☐
Resten av året	☐	☐	☐	☐	☐

Hvilken type kapsler/piller med tran/omega-3/fiskeolje bruker du vanligvis, og hvor mange pleier du å ta hver gang?

Navn ..... Antall ☐☐

Navn ..... Antall ☐☐

Navn ..... Antall ☐☐

KOSTTILSKUDD

Bruker du kosttilskudd?

☐ Ja ☐ Nei

Hvis JA, hvor ofte bruker du kosttilskudd? (Sett ett kryss pr. linje)

Navn på kosttilskudd	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2-6 pr. uke	daglig
.....	☐	☐	☐	☐	☐
.....	☐	☐	☐	☐	☐
.....	☐	☐	☐	☐	☐
.....	☐	☐	☐	☐	☐

KOSTHOLD

Påvirker noen av følgende forhold kostholdet ditt?
(Sett om nødvendig flere kryss)

☐ Er vegetarianer/veganer
☐ Spiser ikke norsk kost til daglig
☐ Har allergi/intoleranse
☐ Kronisk sykdom
☐ Har anoreksi
☐ Har bulimi
☐ Prøver å gå ned i vekt
☐ Lav glykemisk mat

Vi er interessert i å få kjennskap til hvordan kostholdet ditt er vanligvis. Kryss av for hvert spørsmål om hvor ofte du i gjennomsnitt siste året har brukt den aktuelle matvaren, og hvor mye du pleier å spise/drikke hver gang.

DRIKKE

Hvor mange glass melk drikker du vanligvis av hver type?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1-4 pr. uke	5-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Helmelk *(søt, sur)*	☐	☐	☐	☐	☐	☐
Lettmelk *(søt, sur)*	☐	☐	☐	☐	☐	☐
Ekstra lettmelk	☐	☐	☐	☐	☐	☐
Skummet *(søt, sur)*	☐	☐	☐	☐	☐	☐

Hvor mange kopper kaffe/te drikker du vanligvis av hver sort?
(Sett ett kryss for hver linje)

	aldri/ sjelden	1-6 pr. uke	1 pr. dag	2-3 pr. dag	4-5 pr. dag	6-7 pr. dag	8+ pr. dag
Kokekaffe	☐	☐	☐	☐	☐	☐	☐
Traktekaffe	☐	☐	☐	☐	☐	☐	☐
Pulverkaffe	☐	☐	☐	☐	☐	☐	☐
Presskanne kaffe	☐	☐	☐	☐	☐	☐	☐
Anne kaffe *(latte, espresso ol.)*	☐	☐	☐	☐	☐	☐	☐
Svart te	☐	☐	☐	☐	☐	☐	☐
Grønn te	☐	☐	☐	☐	☐	☐	☐

Bruker du følgende i kaffe eller te:

	Kaffe		Te	
Sukker *(ikke kunstig søtstoff)*	☐ Ja	☐ Nei	☐ Ja	☐ Nei
Melk eller fløte	☐ Ja	☐ Nei	☐ Ja	☐ Nei

Hvor mange glass vann drikker du vanligvis?

	aldri/ sjelden	1-6 pr. uke	1 pr. dag	2-3 pr. dag	4-5 pr. dag	6-7 pr. dag	8+ pr. dag
Springvann/flaskevann	☐	☐	☐	☐	☐	☐	☐

Hvor mange glass juice, saft og brus drikker du vanligvis?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. uke	4-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Appelsinjuice	☐	☐	☐	☐	☐	☐
Annen juice	☐	☐	☐	☐	☐	☐
Saft/brus med sukker	☐	☐	☐	☐	☐	☐
Saft/brus sukkerfri	☐	☐	☐	☐	☐	☐

YOGHURT/KORNBLANNING

Hvor ofte spiser du yoghurt (1 beger)? (Sett ett kryss)

☐ Aldri/sjelden
☐ 1 pr. uke
☐ 2-3 pr. uke
☐ 4+ pr. uke

Hvor ofte spiser du kornblanding, havregryn eller müsli?
(Sett ett kryss)

☐ Aldri/sjelden
☐ 1-3 pr. uke
☐ 4-6 pr. uke
☐ 1+ pr. dag

BRØDMAT

Hvor mange skiver brød/rundstykker og knekkebrød/ skonrokker spiser du vanligvis?
(1/2 rundstykke = 1 brødskive) (Sett ett kryss for hver linje)

	aldri/ sjelden	1-4 pr. uke	5-7 pr. uke	2-3 pr. dag	4-5 pr. dag	6+ pr. dag
Grovbrød	☐	☐	☐	☐	☐	☐
Kneip/halvfint	☐	☐	☐	☐	☐	☐
Fint brød/baguett	☐	☐	☐	☐	☐	☐
Knekkebrød o.l.	☐	☐	☐	☐	☐	☐

Nedenfor er det spørsmål om bruk av ulike påleggstyper. Vi spør om hvor mange brødskiver med det aktuelle pålegget du pleier å spise. Dersom du også bruker matvarene i andre sammenhenger enn til brød (f. eks. til vafler, frokostblandinger, grøt), ber vi om at du tar med dette når du besvarer spørsmålene.

På hvor mange brødskiver bruker du? (Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. uke	4-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Syltetøy	☐	☐	☐	☐	☐	☐
Brunost helfet	☐	☐	☐	☐	☐	☐
Brunost halvfet/mager	☐	☐	☐	☐	☐	☐
Hvitost helfet	☐	☐	☐	☐	☐	☐
Hvitost halvfet/mager	☐	☐	☐	☐	☐	☐
Kjøttpålegg, leverpostei	☐	☐	☐	☐	☐	☐
Rekesalat, italiensk o.l.	☐	☐	☐	☐	☐	☐

På hvor mange brødskiver pr. uke har du i gjennomsnitt siste året spist? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7-9 pr. uke	10+ pr. uke
Makrell i tomat, røkt makrell	☐	☐	☐	☐	☐	☐
Kaviar	☐	☐	☐	☐	☐	☐
Sild/ansjos/sardiner	☐	☐	☐	☐	☐	☐
Laks/ørret *(gravet/røkt)*	☐	☐	☐	☐	☐	☐
Svolværpostei/Lofotpostei	☐	☐	☐	☐	☐	☐
Krabbepålegg	☐	☐	☐	☐	☐	☐
Annet fiskepålegg	☐	☐	☐	☐	☐	☐

Hva slags fett bruker du vanligvis på brødet?

- ☐ Bruker ikke fett på brødet
- ☐ Smør
- ☐ Hard margarin *(f. eks. Per, Melange)*
- ☐ Myk margarin *(f. eks. Soft, Vita, Solsikke)*
- ☐ Smørblandet margarin *(f.eks. Bremyk)*
- ☐ Brelett
- ☐ Lettmargarin *(f. eks. Soft light, Letta, Vita Lett)*
- ☐ Middels lett margarin *(f. eks. Olivero, Omega)*

Dersom du bruker fett på brødet, hvor tykt lag pleier du å smøre på? (En kuvertpakke med margarin veier 12 gram).
(Sett ett kryss)

- ☐ Skrapet (3 g)
- ☐ Tynt lag (5 g)
- ☐ Godt dekket (8 g)
- ☐ Tykt lag (12 g)

FRUKT OG GRØNNSAKER

Hvor ofte spiser du frukt? (Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2-4 pr. uke	5-6 pr uke	1 pr dag	2+ pr dag
Epler/pærer	☐	☐	☐	☐	☐	☐	☐
Appelsiner o.l.	☐	☐	☐	☐	☐	☐	☐
Bananer	☐	☐	☐	☐	☐	☐	☐
Annen frukt	☐	☐	☐	☐	☐	☐	☐

Hvor ofte spiser du ulike typer grønnsaker? (Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2 pr. uke	3 pr uke	4-5 pr uke	6-7 pr uke
Gulrøtter	☐	☐	☐	☐	☐	☐	☐
Kål	☐	☐	☐	☐	☐	☐	☐
Kålrot	☐	☐	☐	☐	☐	☐	☐
Brokkoli/blomkål	☐	☐	☐	☐	☐	☐	☐
Blandet salat	☐	☐	☐	☐	☐	☐	☐
Tomat	☐	☐	☐	☐	☐	☐	☐
Grønnsakblanding *(frossen)*	☐	☐	☐	☐	☐	☐	☐
Løk	☐	☐	☐	☐	☐	☐	☐
Andre grønnsaker	☐	☐	☐	☐	☐	☐	☐

For de grønnsakene du spiser, kryss av for hvor mye du spiser hver gang: (Sett ett kryss for hver sort):

Gulrøtter *(stk)*	☐ ½	☐ 1	☐ 1 ½	☐ 2+
Kål *(dl)*	☐ ½	☐ 1	☐ 1 ½	☐ 2+
Kålrot *(dl)*	☐ ½	☐ 1	☐ 1 ½	☐ 2+
Brokkoli/blomkål *(buketter)*	☐ 1-2	☐ 3-4	☐ 5+	
Blandet salat *(dl)*	☐ 1	☐ 2	☐ 3	☐ 4+
Tomat *(stk)*	☐ ¼	☐ ½	☐ 1	☐ 2+
Grønnsakblanding *(frossen) (dl)*	☐ ½	☐ 1	☐ 2	☐ 3+

Hvor mange poteter spiser du vanligvis (kokte, stekte, mos)?
(Sett ett kryss)

- ☐ Aldri/sjelden
- ☐ 1-4 pr uke
- ☐ 5-6 pr. uke
- ☐ 1 pr dag
- ☐ 2 pr dag
- ☐ 3 pr dag
- ☐ 4+ pr dag

RIS, SPAGHETTI, GRØT, SUPPE

Hvor ofte bruker du ris og spaghetti/makaroni?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2 pr. uke	3+ pr uke
Ris	☐	☐	☐	☐	☐
Spaghetti, makaroni, nudler	☐	☐	☐	☐	☐

Hvor ofte spiser du grøt?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2-6 pr. uke	1+ pr. dag
Risengrynsgrøt	☐	☐	☐	☐	☐	☐
Annen grøt *(havre o.l.)*	☐	☐	☐	☐	☐	☐

Hvor ofte spiser du suppe?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2 pr. uke	3+ pr uke
Som hovedrett	☐	☐	☐	☐	☐
Som forrett, lunsj eller kveldsmat	☐	☐	☐	☐	☐

FISK

Vi vil gjerne vite hvor ofte du pleier å spise fisk, og ber deg fylle ut spørsmålene om fiskeforbruk så godt du kan. Tilgangen på fisk kan variere gjennom året. Vær vennlig å markere i hvilke årstider du spiser de ulike fiskeslagene.

	aldri/ sjelden	like mye hele året	vinter	vår	sommer	høst
Torsk, sei, hyse, lyr	☐	☐	☐	☐	☐	☐
Steinbit, flyndre, uer	☐	☐	☐	☐	☐	☐
Laks, ørret	☐	☐	☐	☐	☐	☐
Kveite	☐	☐	☐	☐	☐	☐
Makrell	☐	☐	☐	☐	☐	☐
Sild	☐	☐	☐	☐	☐	☐
Tunfisk *(ikke på boks)*	☐	☐	☐	☐	☐	☐
Ferskvannsfisk (*Abbor, gjedde, røye, sik, harr)*	☐	☐	☐	☐	☐	☐
Annen fisk	☐	☐	☐	☐	☐	☐

Med tanke på de periodene av året der du spiser fisk, hvor ofte pleier du å spise følgende til middag? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2+ pr uke
Kokt torsk, sei, hyse, lyr	☐	☐	☐	☐	☐
Stekt torsk, sei, hyse, lyr	☐	☐	☐	☐	☐
Steinbit, flyndre, uer	☐	☐	☐	☐	☐
Laks, ørret	☐	☐	☐	☐	☐
Kveite	☐	☐	☐	☐	☐
Makrell	☐	☐	☐	☐	☐
Sild	☐	☐	☐	☐	☐
Tunfisk *(ikke på boks)*	☐	☐	☐	☐	☐
Ferskvannsfisk (*Abbor, gjedde, røye, sik, harr)*	☐	☐	☐	☐	☐
Annen fisk	☐	☐	☐	☐	☐

Dersom du spiser fisk, hvor mye spiser du vanligvis pr. gang? (1 skive/stykke = 150 gram)

Kokt fisk *(skive)*	☐ 1	☐ 1,5	☐ 2	☐ 3+
Stekt fisk *(stykke)*	☐ 1	☐ 1,5	☐ 2	☐ 3+

Hvor mange ganger pr. år spiser du fiskeinnmat? (Sett ett kryss for hver linje)

	aldri	1-3	4-6	7-9	10-15	16+
Rogn	☐	☐	☐	☐	☐	☐
Fiskelever	☐	☐	☐	☐	☐	☐

Dersom du spiser fiskelever, hvor mange spiseskjeer pleier du å spise hver gang? (Sett ett kryss)

☐ 1 ☐ 2 ☐ 3-4 ☐ 5-6 ☐ 7+

Hvor ofte bruker du følgende typer fiskemat? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2+ pr uke
Fiskekaker/pudding/boller	☐	☐	☐	☐	☐
Plukkfisk/fiskegrateng	☐	☐	☐	☐	☐
Frityrfisk/fiskepinner	☐	☐	☐	☐	☐
Andre fiskeretter	☐	☐	☐	☐	☐

Hvor stor mengde pleier du vanligvis å spise av de ulike rettene? (Sett ett kryss for hver linje)

Fiskekaker/pudding/boller *(stk.)* *(2 fiskeboller=1 fiskekake)*	☐ 1	☐ 2	☐ 3	☐ 4+
Plukkfisk, fiskegrateng *(dl)*	☐ 1-2	☐ 3-4	☐ 5+	
Frityrfisk, fiskepinner *(stk.)*	☐ 1-2	☐ 3-4	☐ 5-6	☐ 7+

I tillegg til informasjon om fiskeforbruk er det viktig å få kartlagt hvilket tilbehør som blir servert til fisk.
Hvor ofte bruker du følgende til fisk? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2+ pr uke
Smeltet/fast smør	☐	☐	☐	☐	☐
Smeltet/fast margarin/fett	☐	☐	☐	☐	☐
Seterrømme *(35%)*	☐	☐	☐	☐	☐
Lettrømme *(20%)*	☐	☐	☐	☐	☐
Saus med fett *(hvit/brun)*	☐	☐	☐	☐	☐
Saus uten fett *(hvit/brun)*	☐	☐	☐	☐	☐

For de ulike typene tilbehør du bruker til fisk, vær vennlig å kryss av for hvor mye du vanligvis pleier å spise.

Smeltet/fast smør *(ss)*	☐ ½	☐ 1	☐ 2	☐ 3	☐ 4+
Smeltet/fast margarin *(ss)*	☐ ½	☐ 1	☐ 2	☐ 3	☐ 4+
Seterrømme *(ss)*	☐ ½	☐ 1	☐ 2	☐ 3	☐ 4+
Lettrømme *(ss)*	☐ ½	☐ 1	☐ 2	☐ 3	☐ 4+
Saus med fett *(dl)*	☐ ¼	☐ ½	☐ ¾	☐ 1	☐ 2+
Saus uten fett *(dl)*	☐ ¼	☐ ½	☐ ¾	☐ 1	☐ 2+

Hvor mange ganger i året spiser du hval-/selkjøtt? (Sett ett kryss)

aldri	1-3	4-6	7-9	10-15	16+
☐	☐	☐	☐	☐	☐

Hvor mange ganger i året spiser du det brune kjøttet i krabbe (utenom krabbepålegg)? (Sett ett kryss)

aldri	1-3	4-6	7-9	10-15	16+
☐	☐	☐	☐	☐	☐

Hvor mange ganger i året spiser du andre skalldyr (reker og skjell)? (Sett ett kryss)

aldri	1-3	4-6	7-9	10-15	16+
☐	☐	☐	☐	☐	☐

Hvor mange måseegg eller egg fra annen sjøfugl spiser du i året? (Sett ett kryss)

aldri	1-3	4-6	7-9	10-15	16+
☐	☐	☐	☐	☐	☐

KJØTT

Hvor ofte spiser du følgende viltprodukter? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2-3 pr. uke	4+ pr. uke
Reinkjøtt	☐	☐	☐	☐	☐	☐
Andre matvarer fra rein *(lever, nyre, margebein, hjerte, tunge, blod og annet)*	☐	☐	☐	☐	☐	☐
Elgkjøtt, andre matvarer fra elg	☐	☐	☐	☐	☐	☐
Rype, annen viltfugl	☐	☐	☐	☐	☐	☐

Hvor ofte spiser du følgende kjøtt- og fjærkreretter? (Sett ett kryss for hver rett)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2+ pr uke
Steik *(okse, svin, får)*	☐	☐	☐	☐	☐
Koteletter	☐	☐	☐	☐	☐
Biff	☐	☐	☐	☐	☐
Kjøttkaker, karbonader	☐	☐	☐	☐	☐
Pølser	☐	☐	☐	☐	☐
Gryterett, lapskaus	☐	☐	☐	☐	☐
Pizza med kjøtt	☐	☐	☐	☐	☐
Kylling	☐	☐	☐	☐	☐
Bacon, flesk	☐	☐	☐	☐	☐
Innmat får/storfe	☐	☐	☐	☐	☐
Andre kjøttretter	☐	☐	☐	☐	☐

Dersom du spiser følgende retter, oppgi mengden du vanligvis spiser: (Sett ett kryss for hver linje)

Steik *(skiver)*	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5+
Koteletter *(stk.)*	☐ ½	☐ 1	☐ 1 ½	☐ 2+	
Kjøttkaker, karbonader *(stk)*	☐ 1	☐ 2	☐ 3	☐ 4+	
Pølser *(stk à 150g)*	☐ ½	☐ 1	☐ 1 ½	☐ 2+	
Gryterett, lapskaus *(dl)*	☐ 1-2	☐ 3	☐ 4	☐ 5+	
Pizza m/kjøtt *(stykke à 100 g)*	☐ 1	☐ 2	☐ 3	☐ 4+	

Hvilke sauser bruker du til kjøttretter og pastaretter?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2+ pr uke
Brun saus	☐	☐	☐	☐	☐
Sjysaus	☐	☐	☐	☐	☐
Tomatsaus	☐	☐	☐	☐	☐
Saus med fløte/rømme	☐	☐	☐	☐	☐

Hvor mye bruker du vanligvis av disse sausene?
(Sett ett kryss for hver linje)

Brun saus *(dl)*	☐ ¼	☐ ½	☐ ¾	☐ 1	☐ 2+
Sjysaus *(dl)*	☐ ¼	☐ ½	☐ ¾	☐ 1	☐ 2+
Tomatsaus *(dl)*	☐ ¼	☐ ½	☐ ¾	☐ 1	☐ 2+
Saus med fløte/rømme *(dl)*	☐ ¼	☐ ½	☐ ¾	☐ 1	☐ 2+

ANDRE MATVARER

Hvor mange egg spiser du vanligvis i løpet av en uke (stekte, kokte, eggerøre, omelett)? (Sett ett kryss)

☐ 0 ☐ 1 ☐ 2 ☐ 3-4 ☐ 5-6 ☐ 7+

Hvor ofte spiser du iskrem (til dessert, Krone-is osv.)?
Sett ett kryss for hvor ofte du spiser iskrem om sommeren, og ett kryss for resten av året

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2+ pr uke
Om sommeren	☐	☐	☐	☐	☐
Resten av året	☐	☐	☐	☐	☐

Hvor mye is spiser du vanligvis pr. gang? (Sett ett kryss)

☐ 1 dl ☐ 2 dl ☐ 3 dl ☐ 4+ dl

Hvor ofte spiser du bakevarer som boller, kaker, wienerbrød eller småkaker? (Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2-3 pr. uke	4-6 pr. uke	1+ pr. dag
Gjærbakst *(boller ol.)*	☐	☐	☐	☐	☐	☐
Wienerbrød, kringle	☐	☐	☐	☐	☐	☐
Kaker	☐	☐	☐	☐	☐	☐
Pannekaker	☐	☐	☐	☐	☐	☐
Vafler	☐	☐	☐	☐	☐	☐
Småkaker, kjeks	☐	☐	☐	☐	☐	☐
Lefser, lomper	☐	☐	☐	☐	☐	☐

Hvor ofte spiser du dessert? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2-3 pr. uke	4+ pr. uke
Pudding sjokolade/karamell	☐	☐	☐	☐	☐	☐
Riskrem, fromasj	☐	☐	☐	☐	☐	☐
Kompott, fruktgrøt, hermetisk frukt	☐	☐	☐	☐	☐	☐
Jordbær *(friske, frosne)*	☐	☐	☐	☐	☐	☐
Andre bær *(friske, frosne)*	☐	☐	☐	☐	☐	☐

Hvor ofte spiser/drikker du ville bær, inkludert syltetøy og saft? (Ikke industrifremstilt)? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2-3 pr. uke	4+ pr. uke
Multebær	☐	☐	☐	☐	☐	☐
Tyttebær	☐	☐	☐	☐	☐	☐
Blåbær	☐	☐	☐	☐	☐	☐
Krøkebær	☐	☐	☐	☐	☐	☐
Andre bær	☐	☐	☐	☐	☐	☐

Hvor ofte spiser du selvplukket sopp? (Sett ett kryss pr. linje)

aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2-3 pr. uke	4+ pr. uke
☐	☐	☐	☐	☐	☐

Hvor ofte spiser du sjokolade? (Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2-3 pr. uke	4-6 pr. uke	1+ pr. dag
Mørk sjokolade	☐	☐	☐	☐	☐	☐
Lys sjokolade	☐	☐	☐	☐	☐	☐

Dersom du spiser sjokolade, hvor mye pleier du vanligvis å spise hver gang? Tenk deg størrelsen på en Kvikk-Lunsj sjokolade, og oppgi hvor mye du spiser i forhold til den.

☐ ¼ ☐ ½ ☐ ¾ ☐ 1 ☐ 1 ½ ☐ 2+

Hvor ofte spiser du snacks? (Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2-3 pr. uke	4-6 pr. uke	1+ pr. dag
Potetchips	☐	☐	☐	☐	☐	☐
Peanøtter	☐	☐	☐	☐	☐	☐
Andre nøtter	☐	☐	☐	☐	☐	☐
Annen snacks	☐	☐	☐	☐	☐	☐

VARM MAT

Hvor mange ganger i løpet av en måned spiser du varm mat?

Til frokost ☐☐ Til middag ☐☐
Til lunch ☐☐ Til kvelds ☐☐

KOSTHOLD GJENNOM ULIKE LIVSFASER

Det kan være vanskelig å huske eksakt hva du har spist gjennom tiden, men fyll ut sånn omtrent.

Hvor ofte har du spist fisk? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2-3 pr. uke	4+ pr. uke
Barndom	☐	☐	☐	☐	☐	☐
Ungdom 13-19	☐	☐	☐	☐	☐	☐
Voksen *(før siste året)*	☐	☐	☐	☐	☐	☐

Når du har spist fisk, hvor ofte har du da spist fet fisk (laks, ørret, kveite, makrell, sild, ål)? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2-3 pr. uke	4+ pr. uke
Barndom	☐	☐	☐	☐	☐	☐
Ungdom 13-19	☐	☐	☐	☐	☐	☐
Voksen *(før siste året)*	☐	☐	☐	☐	☐	☐

Når du har spist fisk, hvor ofte har du da spist ferskvannsfisk (abbor, gjedde, røye, sik, harr)? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2-3 pr. uke	4+ pr. uke
Barndom	☐	☐	☐	☐	☐	☐
Ungdom 13-19	☐	☐	☐	☐	☐	☐
Voksen *(før siste året)*	☐	☐	☐	☐	☐	☐

Hvor ofte har du spist fiskepålegg (Makrell, sild, ansjos, sardiner, røkt eller gravet laks/ørret, kaviar, fiskeleverpostei (Lofotpostei, Svolværpostei) krabbepålegg)?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2-3 pr. uke	4-6 pr. uke	Daglig
Barndom	☐	☐	☐	☐	☐	☐	☐
Ungdom 13-19	☐	☐	☐	☐	☐	☐	☐
Voksen *(før siste året)*	☐	☐	☐	☐	☐	☐	☐

Hvor mange ganger i året har du spist fiskelever?
(Sett ett kryss pr. linje)

	aldri	1-3	4-6	7-9	10-15	16+
Barndom	☐	☐	☐	☐	☐	☐
Ungdom 13-19	☐	☐	☐	☐	☐	☐
Voksen *(før siste året)*	☐	☐	☐	☐	☐	☐

Hvor mange ganger i året har du spist hval-/selkjøtt?
(Sett ett kryss pr. linje)

	aldri	1-3	4-6	7-9	10-15	16+
Barndom	☐	☐	☐	☐	☐	☐
Ungdom 13-19	☐	☐	☐	☐	☐	☐
Voksen *(før siste året)*	☐	☐	☐	☐	☐	☐

Hvor mange ganger i året har du spist det brune kjøttet i krabbe (utenom krabbepålegg)? (Sett ett kryss pr. linje)

	aldri	1-3	4-6	7-9	10-15	16+
Barndom	☐	☐	☐	☐	☐	☐
Ungdom 13-19	☐	☐	☐	☐	☐	☐
Voksen *(før siste året)*	☐	☐	☐	☐	☐	☐

Hvor mange måseegg eller egg fra annen sjøfugl har du spist i året? (Sett ett kryss pr. linje)

	aldri	1-3	4-6	7-9	10-15	16+
Barndom	☐	☐	☐	☐	☐	☐
Ungdom 13-19	☐	☐	☐	☐	☐	☐
Voksen *(før siste året)*	☐	☐	☐	☐	☐	☐

Hvor ofte i nevnte livsfaser har du tatt tilskudd av tran/ omega-3/fiskeolje (flytende/kapsler/piller)?
(Sett ett kryss pr. linje)

	Aldri	1-3 pr. mnd.	1 pr. uke	2-6 pr. uke	Daglig
Barndom vinter	☐	☐	☐	☐	☐
Barndom resten av året	☐	☐	☐	☐	☐
Ungdom 13-19 vinter	☐	☐	☐	☐	☐
Ungdom 13-19 resten av året	☐	☐	☐	☐	☐
Voksen vinter *(før siste året)*	☐	☐	☐	☐	☐
Voksen resten av året *(før siste året)*	☐	☐	☐	☐	☐

BARNEFAR

I forbindelse med sammenligning av ultralydmål, er det viktig å ha noen opplysninger om far til barnet i dette svangerskapet:

Hva var barnefars fødselsvekt som nyfødt baby?
(Gram) ☐☐☐☐ Vet ikke ☐

Hva er barnefars høyde i dag? *(cm)* ☐☐☐ Vet ikke ☐

Hvilket hjemmespråk har/hadde barnefar, hans foreldre og hans besteforeldre? (sett ett eller flere kryss)

	Norsk	Samisk	Kvensk	Annet	Vet ikke	Dersom annet beskriv
Morfar	☐	☐	☐	☐	☐	
Mormor	☐	☐	☐	☐	☐	
Farfar	☐	☐	☐	☐	☐	
Farmor	☐	☐	☐	☐	☐	
Far	☐	☐	☐	☐	☐	
Mor	☐	☐	☐	☐	☐	
Barnefar	☐	☐	☐	☐	☐	

Hva er barnefars, hans fars og hans mors etniske bakgrunn?
(sett ett eller flere kryss)

	Norsk	Samisk	Kvensk	Annet	Vet ikke	Dersom annet beskriv
Barnefars bakgrunn	☐	☐	☐	☐	☐	
Mors bakgrunn	☐	☐	☐	☐	☐	
Fars bakgrunn	☐	☐	☐	☐	☐	

Hva regner barnefar seg selv som? (sett ett eller flere kryss)

Norsk	Samisk	Kvensk	Annet	Vet ikke	Dersom annet beskriv
☐	☐	☐	☐	☐	

ANGÅENDE SPØRSMÅLENE

Var noen av spørsmålene vanskelige eller nærgående? Hvis ja oppgi hvilke spørsmål og evt. kommentarer.

☐ Ja ☐ Nei

Andre kommentarer:

Takk for hjelpen!

Vinter 2005

KVINNER OG KREFT

KONFIDENSIELT

Vi ber deg fylle ut spørreskjemaet så nøye som mulig.
Dersom du ikke ønsker å delta kan du unngå purring ved å sette kryss for NEI og returnere skjemaet i vedlagte svarkonvolutt.

Skjemaet skal leses optisk. Vennligst bruk blå eller sort penn.
Du kan ikke bruke komma, bruk blokkbokstaver.

Med vennlig hilsen
Eiliv Lund
Professor dr. med

Jeg samtykker i å delta i spørreskjemaundersøkelsen JA ☐ NEI ☐

Sosiale forhold

Er du: (Sett ett kryss)
☐ gift ☐ samboer ☐ ugift ☐ skilt ☐ enke

Hvor mange års skolegang/yrkesutdannelse har du i alt, ta med folkeskole og ungdomsskole? ☐

Hvor mange personer er det i ditt hushold? ☐

Hvor høy er bruttoinntekten i husholdet pr. år?

under 150.000 kr.	☐	151.000-300.000 kr.	☐
301.000-450.000 kr.	☐	451.000-600.000 kr.	☐
601.000-750.000 kr.	☐	over 750.000 kr.	☐

Hva er din arbeidssituasjon? (sett kryss)
☐ Arbeider heltid ☐ Arbeider deltid ☐ Pensjonist
☐ Hjemmearbeidende ☐ Under utdanning ☐ Uføretrygdet
☐ Under attføring ☐ Arbeidssøkende

Yrke: ☐

Høyde og vekt

Hvor høy er du? (i hele cm.) ☐

Hvor mye veide du da du var 18 år? (i hele kg.) ☐

Hvor mye veier du i dag? (i hele kg.) ☐

Kroppstype i 1. klasse. (Sett ett kryss)
☐ veldig tynn ☐ tynn ☐ normal ☐ tykk ☐ veldig tykk

Menstruasjonsforhold

Hvor gammel var du da du fikk menstruasjon første gang? ☐

Hvor mange år tok det før menstruasjonen ble regelmessig?
☐ Ett år eller mindre ☐ Mer enn ett år
☐ Aldri ☐ Husker ikke

Overgangsalder

Har du regelmessig menstruasjon fremdeles?
☐ Ja ☐ Har uregelmessig menstruasjon
☐ Vet ikke (menstruasjon uteblitt pga. sykdom o.l.)
☐ Bruk av hormonpreparat med østrogen
☐ Nei

Hvis Nei;
har den stoppet av seg selv? ☐
operert vekk eggstokkene? ☐
operert vekk livmoren? ☐
annet? ☐

Alder da menstruasjonen opphørte? ☐

Graviditeter, fødsler og amming

Har du noen gang vært gravid? Ja ☐ Nei ☐

Hvis Ja; fyll ut for hvert barn du har født opplysninger om fødselsår og antall måneder du ammet (fylles også ut for dødfødte eller for barn som er døde senere i livet). Dersom du ikke har født barn fortsetter du ved neste spørsmål.

Barn	Fødselsår	Antall måneder med amming	Barn	Fødselsår	Antall måneder med amming
1	☐	☐	5	☐	☐
2	☐	☐	6	☐	☐
3	☐	☐	7	☐	☐
4	☐	☐	8	☐	☐

Bruk av hormonpreparater med østrogen i overgangsalderen

Har du noen gang brukt østrogen-tabletter/plaster? Ja ☐ Nei ☐

Hvis Ja; hvor mange år har du brukt østrogentabletter/plaster i alt? ☐

Hvor gammel var du første gang du brukte østrogentabletter/plaster? ☐

Bruker du tabletter/plaster nå? Ja ☐ Nei ☐

UTFYLLENDE SPØRSMÅL TIL ALLE SOM HAR BRUKT ELLER BRUKER PREPARATER MED ØSTROGEN I FORM AV TABLETTER ELLER PLASTER.

Hvis du har svart «nei» på spørsmålene om hormonbruk i overgangsalderen, kan du gå videre til spørsmålene under «**P-pillebruk**». Har du svart «ja», ber vi deg utdype dette nærmere ved å svare på spørsmålene nedenfor. For hver periode med sammenhengende bruk av samme hormonpreparat håper vi du kan si oss hvor gammel du var da du startet, hvor lenge du brukte det samme hormonpreparatet og navnet på dette. Dersom du har hatt opphold eller skiftet merke skal du besvare spørsmålene for en ny periode. Dersom du ikke husker navnet på hormonpreparatet, sett «usikker». For å hjelpe deg til å huske navnet på hormonpreparatene ber vi deg bruke den vedlagte brosjyre som viser bilder av hormonpreparater som har vært solgt i Norge. Vennligst oppgi også nummer på hormontabletten/plasteret som står i brosjyren.

Periode	Alder ved start	Brukt samme hormontablett/plaster/ sammenhengende år	måned	Nr.	Navn på hormontablett/ plaster/ (se brosjyre)
1.					
	Angi nr. her dersom du bruker to preparater				
2					
	Angi nr. her dersom du bruker to preparater				
3.					
	Angi nr. her dersom du bruker to preparater				

P-pillebruk

Har du brukt p-piller eller minipiller? ..... Ja ☐ Nei ☐

Hvis ja, hvor mange år har du brukt p-piller i alt .....

Bruker du p-piller nå? ..... Ja ☐ Nei ☐

For p-pillebruk ønsker vi å få vite navnet på p-pillen, årstallet du startet å bruke den og hvor lenge du brukte dette merket sammenhengende. Dersom du har hatt opphold eller skiftet merke start på ny linje. For å hjelpe deg å huske navnet ber vi deg bruke den vedlagte brosjyren. Vennligst oppgi nummeret på p-pillen.

Periode	Alder ved start	Brukt samme p-piller sammenhengende år	måned	Nr.	P-piller (se brosjyre) Navn
1.					
2.					
3.					
4.					

Hormonspiral

Har du noen gang brukt hormonspiral (Levonova)? ..... Ja ☐ Nei ☐

Hvis Ja; hvor mange hele år har du brukt hormonspiral i alt? .....

Hvor gammel var du første gang du fikk innsatt hormonspiral?

Bruker du hormonspiral nå? ..... Ja ☐ Nei ☐

Østrogenpreparat til lokal bruk i skjeden

Har du noen gang brukt østrogen-krem/stikkpille? ..... Ja ☐ Nei ☐

Hvis Ja; bruker du krem/stikkpille nå? ..... Ja ☐ Nei ☐

Andre legemidler

Bruker du noen av disse legemidlene daglig nå?

Fontex, Fluoxetin ..... Ja ☐ Nei ☐

Cipramil, Citalopram, Desital ..... Ja ☐ Nei ☐

Seroxat, Paroxetin ..... Ja ☐ Nei ☐

Zoloft ..... Ja ☐ Nei ☐

Fevarin ..... Ja ☐ Nei ☐

Cipralex ..... Ja ☐ Nei ☐

Hvis Ja; hvor lenge har du brukt dette legemidlet sammenhengede? Måneder ____ År ____

Har du benyttet noen av disse legemidlene tidligere? Ja ☐ Nei ☐

Hvis Ja; hvor lenge har du benyttet disse legemidlene i alt? År ____

Sykdom

Har du eller har du hatt noen av følgende sykdommer?

	Ja	Nei	Hvis ja: Alder ved start
Kreft	☐	☐	
Høyt blodtrykk	☐	☐	
Hjertesvikt/hjertekrampe	☐	☐	
Hjerteinfarkt	☐	☐	
Slag	☐	☐	
Sukkersyke (diabetes)	☐	☐	
Depresjon (oppsøkt lege)	☐	☐	

Røykevaner

Har du i løpet av livet røykt mer enn 100 sigaretter til sammen? Ja ☐ Nei ☐

Hvor gammel var du da du tok din første sigarett? ☐

Hvis Ja, ber vi deg om å fylle ut for hver aldersgruppe i livet hvor mange sigaretter du i gjennomsnitt røykte pr. dag i den perioden.

Antall sigaretter hver dag

Alder	0	1-4	5-9	10-14	15-19	20-24	25+
10-14	☐	☐	☐	☐	☐	☐	☐
15-19	☐	☐	☐	☐	☐	☐	☐
20-29	☐	☐	☐	☐	☐	☐	☐
30-39	☐	☐	☐	☐	☐	☐	☐
40-49	☐	☐	☐	☐	☐	☐	☐
50+	☐	☐	☐	☐	☐	☐	☐

	Ja	Nei
Røyker du daglig nå?	☐	☐
Røykte noen av dine foreldre da du var barn?	☐	☐

Hvis Ja, hvor mange sigaretter røykte de til sammen pr. dag? ☐

Brystkreft i nærmeste familie

Har noen nære slektninger hatt brystkreft?

	Ja	Nei	Vet ikke	Alder ved start
Din datter	☐	☐	☐	☐
Din mor	☐	☐	☐	☐
Din søster	☐	☐	☐	☐

Hvor mange søstre har du (ta med evt. døde) ☐

Hvor mange døtre har du (ta med evt. døde) ☐

Selvopplevd helse

Oppfatter du din egen helse som; (Sett ett kryss)

Meget god ☐ God ☐ Dårlig ☐ Meget dårlig

Mammografiundersøkelse

Har du vært til undersøkelse av brystene med mammografi Nei ☐ Ja ☐

Hvis Ja;
hvor mange år er det siden du sist var til mammografi? (hele år) ☐

Har du hatt noen form for operasjon av bryst(ene)? **Alder (år)**

Godartet kul (angi alder for første gang) ☐

Brystreduksjon (angi alder) ☐

Brystinnlegg (silikon) ☐

Annet (angi) ☐

Fysisk aktivitet

Vi ber deg angi din fysiske aktivitet etter en skala fra svært lite til svært mye. Skalaen nedenfor går fra 1-10. Med fysisk aktivitet mener vi både arbeid i hjemmet og i yrkeslivet, samt trening og annen fysisk aktivitet som turgåing o.l. Sett kryss over det tallet som best angir ditt nivå av fysisk aktivitet.

Alder	Svært lite									Svært mye
14 år	1	2	3	4	5	6	7	8	9	10
30 år	1	2	3	4	5	6	7	8	9	10
I dag	1	2	3	4	5	6	7	8	9	10

Hvor mange timer pr. dag i gjennomsnitt går eller spaserer du utendørs?

	sjelden/ aldri	mindre enn 1/2 time	1/2-1 time	1-2 timer	mer enn 2 timer
Vinter	☐	☐	☐	☐	☐
Vår	☐	☐	☐	☐	☐
Sommer	☐	☐	☐	☐	☐
Høst	☐	☐	☐	☐	☐

Alkohol

Er du totalavholdskvinne? Ja ☐ Nei ☐

Hvis Nei; hvor ofte og hvor mye drakk du i gjennomsnitt siste året? (Sett ett kryss for hver linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2-4 pr. uke	5-6 pr. uke	1 pr. dag	2+ pr. dag
Øl (1/2 l.)	☐	☐	☐	☐	☐	☐	☐	☐
Vin (glass)	☐	☐	☐	☐	☐	☐	☐	☐
Brennevin (drink)	☐	☐	☐	☐	☐	☐	☐	☐
Likør/Hetvin (glass)	☐	☐	☐	☐	☐	☐	☐	☐

Solvaner

Får du fregner når du soler deg? Ja ☐ Nei ☐

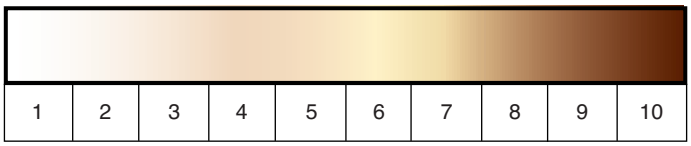
Hvilken øyefarge har du? (sett ett kryss)

☐ brun ☐ grå, grønn eller blanding ☐ blå

Hva er din opprinnelige hårfarge? (sett ett kryss)

☐ mørkbrun, svart ☐ brun ☐ blond, gul ☐ rød

For å kunne studere effekten av soling på risiko for hudkreft ber vi deg gi opplysninger om hudfarge
Sett ett kryss på det tallet under fargen som best passer din naturlige hudfarge (uten soling)



1	2	3	4	5	6	7	8	9	10

Hvor mange ganger pr. år er du blitt forbrent av solen slik at du har fått svie og blemmer med avflassing etterpå? (ett kryss for hver aldersgruppe)

Alder	Aldri	Høyst 1 gang pr. år	2-3 g. pr. år	4-5 g. pr. år	6 eller flere ganger
Før 10 år	☐	☐	☐	☐	☐
10-19 år	☐	☐	☐	☐	☐
20-29 år	☐	☐	☐	☐	☐
30-39 år	☐	☐	☐	☐	☐
40+ år	☐	☐	☐	☐	☐

Hvor mange uker soler du deg pr. år i syden?

Alder	Aldri	1 uke	2-3 uker	4-5 uker	6 uker eller mer
Før 10 år	☐	☐	☐	☐	☐
10-19 år	☐	☐	☐	☐	☐
20-29 år	☐	☐	☐	☐	☐
30-39 år	☐	☐	☐	☐	☐
40+ år	☐	☐	☐	☐	☐
Siste 12 mnd.	☐	☐	☐	☐	☐

Hvor mange uker pr. år soler du deg i Norge eller utenfor syden?

Alder	Aldri	1 uke	2-3 uker	4-5 uker	6 uker eller mer
Før 10 år	☐	☐	☐	☐	☐
10-19 år	☐	☐	☐	☐	☐
20-29 år	☐	☐	☐	☐	☐
30-39 år	☐	☐	☐	☐	☐
40+ år	☐	☐	☐	☐	☐
Siste 12 mnd.	☐	☐	☐	☐	☐

Hvor ofte dusjer eller bader du?

	mer enn 1 g. dagl.	1 g. dagl.	4-6 g. pr. uke	2-3 g. pr. uke	1 g. pr. uke	2-3 g. pr. mnd	sjelden/ aldri
Med såpe/shampo	☐	☐	☐	☐	☐	☐	☐
Uten såpe/shampo	☐	☐	☐	☐	☐	☐	☐

Når bruker du krem med solfaktor? (sett evt. flere kryss):

☐ i påsken ☐ i Norge eller utenfor syden ☐ solferie i syden ☐ aldri

Hvilken solfaktor bruker du i disse periodene?

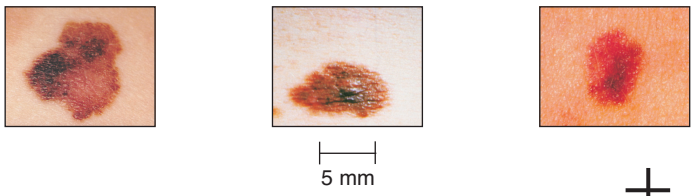
	påsken	i Norge eller utenfor syden	solferie i syden
I dag			
For 10 år siden			

Hvor ofte har du solt deg i solarium?

Alder	Aldri	Sjelden	1 gang pr. mnd.	2 ganger pr. mnd.	3-4 ganger pr. mnd	oftere enn1 gang pr. uke
Før 10 år	☐	☐	☐	☐	☐	☐
10-19 år	☐	☐	☐	☐	☐	☐
20-29 år	☐	☐	☐	☐	☐	☐
30-39 år	☐	☐	☐	☐	☐	☐
40+ år	☐	☐	☐	☐	☐	☐
Siste 12 mnd.	☐	☐	☐	☐	☐	☐

Hvor mange uregelmessige føflekker større enn 5 mm har du sammenlagt på begge beina (fra tærne til lysken)? Tre eksempler på føflekker større enn 5 mm med uregelmessig form er vist i nedenfor.

☐ 0 ☐ 1 ☐ 2-3 ☐ 4-6 ☐ 7-12 ☐ 13-24 ☐ 25+



Hvor ofte bruker du følgende hudpleiemidler?

(Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr.mnd.	1 pr.uke	2-4 pr.uke	5-6 pr.uke	1 pr.dag	2+ pr. dag
Ansiktskrem	☐	☐	☐	☐	☐	☐	☐
Håndkrem	☐	☐	☐	☐	☐	☐	☐
Body lotion	☐	☐	☐	☐	☐	☐	☐
Parfyme	☐	☐	☐	☐	☐	☐	☐

Til slutt vil vi spørre deg om ditt samtykke til å kontakte deg på nytt pr. post. Vi vil hente adressen fra det sentrale personregister.

Ja ☐ Nei ☐

Er du villig til å avgi en blodprøve?

Ja ☐ Nei ☐

Takk for at du ville delta i undersøkelsen

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