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# Risk versus Benefits of Whale and Seal Consumption

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Organizer and coordinator: Hóraldur Joensen



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Bústaður / Address Nóatún 3, FO 100 Tórshavn, Føroyar (Faroe Islands)

Postúrúm / P.O. box 2109, FO 165 Argir, Føroyar (Faroe Islands)

] • 📠 • @ +298 352550 • +298 352551 • nvd@setur.fo



# **Risks versus Benefits of Whale and Seal Consumption**

## **Workshop report**



**14 January 2011  
North Atlantic House  
Copenhagen  
Denmark**

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The project was coordinated by  
The Faculty of Science and Technology  
University of Faroe Islands



FRÓÐSKAPARSETUR  
FØROYA

## Participants

**Maria Dam**; Dr. Scient. Head of department of Environment Agency, Tórshavn, Faroe Islands.

**Grace Egeland**; Associate Professor, McGill University, Center for Indigenous Peoples' Nutrition and Environment and School of Dietetics and Human Nutrition, Macdonald Campus, Ste. Anne de Bellevue, Quebec, Canada.

**Edel Oddny Elvevoll**; Professor, Seafood and Nutrition, University of Tromsø, Norway.

**Arja Erkkilä**; PhD, Assistant Professor, Institute of Public Health and Clinical Nutrition University of Eastern Finland, Kuopio, Finland.

**David James**; FAO Fisheries and Aquaculture Department, Rome, Italy.

**Hóraldur Joensen**; University of the Faroe Islands, Tórshavn, Faroe Islands.

**Gert Mulvad**; Researcher, Family physician at the Centre for Primary Health Care in Nuuk, Nuuk, Greenland.

**Sjúrdur F. Olsen**; Professor, Statens Serum Institut, Dept. of Epidemiology Research, Copenhagen, Denmark.

**Guðrún V. Skúladóttir**; Professor, Faculty of Medicine, School of Health Sciences, University of Iceland, Reykjavik, Iceland.

**Jogeir Toppe**; FAO Fish Products and Industry, Fisheries and Aquaculture Department, Rome, Italy.

**Pál Weihe**; Physician, Researcher, Department of Occupational Medicine and Public Health, Tórshavn, Faroe Islands.



Traditional Faroese dish: boiled potatoes, dried whale meat, dried fish, pickled or dry salted blubber.

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## **Risks versus Benefits of Whale and Seal Consumption** **09:00 – 17:00, Friday 14 January 2011**

**14 January 2010**

Nordatlantens Brygge Strandgade 91 1401 København K, Denmark

### **Workshop report**

Organizer and coordinator: Hóraldur Joensen, University of Faroe Islands (UFI)

Chair: Hóraldur Joensen, University of Faroe Islands

Rapporteur: Harald Holst, Nordic Council of Ministers

Editors: David James, FAO, Jogeir Toppe, FAO, Hóraldur Joensen, UFI

#### **Preface**

In January 2010 the joint FAO/WHO Expert Consultation finished an Executive Summary on the Risks and Benefits of Fish Consumption. This subject has been of interest among different food and health related research groups as well as the general population worldwide. For coastal populations in the North Atlantic this issue has been of especially high interest because the condition of the marine resources is so important for livelihoods in these areas. Apart from different finfish and shellfish, whales and seals constitute a significant part of the diet in the North Atlantic fishery nations. However, these marine mammals were not considered by the FAO/WHO Expert Consultation. Due to public concern about the presence of chemical contaminants in marine mammals, the Faroese/Greenlandic/Danish shared presidency of the Nordic Council of Ministers arranged a workshop on the risks and benefits of consumption of meat and blubber/oil of whales and seals.

The intention was to assist governments in advising their populations by providing a framework for assessment of the net health benefits and risks of consuming culinary products from marine mammals.

#### *Goals of the Project*

- 1) To establish the present state of knowledge of the balance between the beneficial and detrimental properties of food products from marine mammals in the North Atlantic.
- 2) To evaluate available information on the risks and benefits by using the method developed and used by FAO/WHO Expert Consultation for seafood consumption.
- 3) To develop a framework that government agencies can use to advise the general public on the risks and benefits by eating meat and blubber products from marine mammals.
- 4) To determine what further studies are needed to validate the positive and negative health effects.

### *Target Group*

The target group of the study and the recommendations are governmental agencies, particularly those concerned with health and food safety, scientists and the general public.

### *Results*

The workshop report gives an overview of recently published literature on nutrients, contaminants, the risks and benefits of consuming food from marine mammals, as well as information about relevant on-going projects and pertinent national/international investigations. Due to a lack of data no clear-cut recommendations on risks and benefits of consuming food products from whales and seals can be made, but there was consensus on the usefulness of the extension of the methodology, developed by the joint FAO/WHO Expert Consultation for the Quantitative Risk Benefit Assessment for Fish, to whales and seals.

### *Utility value*

The valuable aspect of the workshop is a review of papers and books that contain data on nutrient and contaminant levels in a range of North Atlantic whales and seals. Moreover, the report may be used to provide provisional and restricted guidance to national food safety authorities and the Codex Alimentarius Commission in their work on assessing the risks and benefits of consuming dietary products from North Atlantic whales and seals. Finally, the workshop report identifies some of the research/investigations that should necessarily be carried out in the near future to elucidate unclarified issues regarding safe exploitation of marine mammals as a healthy food resource.

After a brief introduction of each member of the project group, oral Power Point supplemented presentations were given by the participants (Appendix 2). Afterwards, each participant provided an abstract of their presentation (Appendix 1)

## Summary of outcomes

### *Vitamins, MUFA and PUFA*

A substantial number of health benefits that are linked to the intake of seafood and marine mammals. Marine mammals are a good source of vitamins A, B, D and E. They are also a good source of the healthy long-chain monounsaturated fatty acids, LC-MUFA, and *n*-3 long-chain polyunsaturated fatty acids, LC-PUFA. PUFA from marine mammals is in many ways superior and seemingly, PUFA's from seal blubber oil might be more effectively absorbed by the body than those from fish oil.

### *Health and PUFA*

The benefits of *n*-3 LC-PUFA consumption on neurodevelopment and prevention of cardiovascular disease have been established in many studies. There is also a positive effect on the prevention of immune and inflammatory diseases, for instance inflammatory bowel disease (IBD) and joint pain. Intake of food rich in *n*-3 PUFA during pregnancy may decrease the risk of allergic diseases such as asthma in the offspring, and is considered positive for the infants' health, since higher birth weight has been associated with a lower risk of diseases later in life. Studies have also shown that marine *n*-3 fatty acids prolong pregnancy and reduce the risk of pre-term birth, and intake of very-long-chain *n*-3 PUFAs during pregnancy and lactation may be favourable for later mental development of children. On the other hand, high doses of *n*-3 LC-PUFA in early pregnancy may increase the risk of developing hypertensive disorders during pregnancy, so moderation is advisable.

### *Cultural and financial importance*

The socio-economic and cultural aspects of whale and seal consumption are very important to the Inuit people, as demonstrated by Grace Egeland and Gert Mulvad. This is especially since imports of industrially produced foods are expected to continue and to take over an increasing part of the food energy supply and also since food insecurity is a problem in many Inuit communities. The traditional diet is culturally and financially very important to the population. It is also of importance in order to provide sufficient nutrients, because in many places the imported food available is generally of poor quality.

### *Adverse health impacts of POPs*

Whales and seals are both high up in the food chain and long-living, and thus they are exposed to high levels of chemicals such as dioxin like compounds (DLCs), DDT and methyl-mercury over a long period. These are so-called environmentally persistent organic pollutants (POPs). Methyl-mercury adversely affects the development of the fetal nervous system and the immune system. Adults who are exposed to methyl-mercury are also more prone to developing Parkinson's disease. Although a high content of POPs, especially methyl-mercury can be found in both whale and seal -meat, -blubber and -oil, these are also rich in selenium, which has the effect of counteracting methyl-mercury

damage. The toxic effects of diets polluted with methyl-mercury but high in selenium are significantly decreased, rather than exacerbated.

*Inadequate data on nutrients and contaminants*

However, information on nutrients and overall nutritional value of whales is scarce. For instance, with the possible exception of fatty acids, the nutrients in pilot whales are very poorly known. It was noted during the discussions that an analysis of pilot whale would not be very expensive to conduct. In fact no extensive adequate public nutrient and contaminant data-base exists in the Faroe Islands and information is limited in other countries.

*Databases, risk management and communication strategies needed*

During the discussion it became clear that the framework used in the Joint FAO/WHO Expert Consultation on the Risks and Benefits of Fish Consumption (<http://www.fao.org/docrep/014/ba0136e/ba0136e00.pdf>) is both relevant and usable. A similar study on whale and seal consumption is also needed. There is also a need to maintain and improve existing databases on specific nutrients and contaminants, particularly methyl-mercury and other POPs, in whale and seal species, and to develop new databases where there is little information. These could be used as the basis to develop and evaluate risk management and communication strategies that both minimize risks and maximize benefits from eating whales and seals. Vulnerable groups of the population can be defined, especially pregnant and nursing women, infants, people who suffer from, or are at risk of suffering from, cardiovascular diseases and heart problems and infants. However, it is important to acknowledge the fact that in the context of the Canadian Arctic risk has a different meaning in marginalized areas where there is food insecurity.

*Utilization of the FAO/WHO Expert Consultation developed methodology*

It was argued during the discussions in this meeting that the Arctic Monitoring and Assessment Programme (AMAP) and the Nordic Council of Ministers could perhaps be a platform for such a study. AMAP already has extensive knowledge of POPs and contaminants in the Arctic. As Jogeir Toppe and David James pointed out in their presentation: “Although the FAO/WHO Consultation specifically excluded the risks and benefits of marine mammal consumption it is felt that the methodology developed by the Consultation for the quantitative risk benefit assessments for fish, could be used as a basis for a similar assessment regarding the consumption of whales and seals”.

## Conclusions

- Consumption of food prepared from marine mammals provides energy, proteins, and a range of essential nutrients, including the healthy long-chain *n-3* polyunsaturated fatty acids (*n-3* LCPUFA<sup>1</sup>). However, mercury from pilot whale meat is found to have an adverse neurological impact on foetuses, adolescents and adults. With the data presently available it is not possible to conduct a valid evaluation of the risks and benefits of marine mammal consumption.
- Intake of food products from marine mammals is part of the cultural traditions of several boreal peoples and in some populations it is a major source of food and essential nutrients.
- Among the general adult boreal population, long-chain *n-3* highly unsaturated fatty acids (*n-3* LCHUFA) and micronutrients from marine mammals increases physical and mental health. Conversely, halogenated organic lipophilic food contaminants, that are sometimes present, are correlated with several detrimental health impacts on septuagenarians.
- Among infants, young children, adolescents, adults and the elderly the available data are currently insufficient to derive a quantitative framework of health risks and benefits of eating marine mammals from the North Atlantic.

## Recommendations

- Establish comprehensive databases on levels of specific nutrients and contaminants in marine mammals consumed in the North Atlantic.
- Develop and evaluate strategies for risk/benefit management and communication that both minimize the risks and maximize the benefits of consuming marine mammals.

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<sup>1</sup> Also referred to as omega-3 LCPUFA

## **Presentations**

### **1. A model for a quantitative risk-benefit assessment of seafood consumption**

Presented by **Jogeir Toppe**, FAO Fish Products and Industry, Fisheries and Aquaculture Department and **David James**, FAO Fisheries and Aquaculture Department

#### **Background**

The 38<sup>th</sup> meeting of the Codex Committee on Food Additives and Contaminants (CCFAC) requested the Codex Alimentarius Commission (CAC), at its 29<sup>th</sup> session in 2006, to seek scientific advice from FAO and WHO on the health benefits of fish consumption comparing those to the health risks associated with the contaminants methyl-mercury (MeHg) and dioxins and dioxin-like PCBs (DLCs) that may be present in fish. The health risks associated with dietary intake of these compounds have previously been assessed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA).

The CAC request was driven by growing public concern regarding the presence of chemical contaminants in fish. This concern has become more apparent in recent years, while during the same period the multiple nutritional benefits of including fish in the diet have become increasingly clear.

The evolving science in this field has led to questions about how much fish should be eaten, and by whom, in order to minimize the risks of chemical exposures and maximize the health benefits. National authorities have been faced with the challenge of communicating complicated and nuanced messages to consumers and also with questions on regulating maximum levels of these chemical contaminants in fish and other foods.

FAO and WHO held an Expert Consultation on the Risks and Benefits of Fish Consumption 25 to 29 January 2010 at FAO Headquarters, Rome, Italy (FAO/WHO, 2011). Seventeen experts in nutrition, toxicology, epidemiology, dietary exposure and risk-benefit assessments discussed the risks and the benefits of fish consumption. Their task was to review data on nutrient and specific chemical (MeHg and DLCs) contaminant levels in a range of fish species, as well as recent scientific literature covering the risks and benefits of fish consumption. The review was used to consider risk-benefit assessments for specific end-points of benefits and risks, including for sensitive groups of the population. The output is intended to provide guidance to national food safety authorities and the Codex Alimentarius Commission in their work on managing risks taking into account the existing data on the benefits of eating fish. The report is available at: (<http://www.fao.org/docrep/014/ba0136e/ba0136e00.pdf>).

Although the FAO/WHO Consultation specifically excluded the risks and benefits of marine mammal consumption it is felt that the methodology developed by the Consultation for the quantitative risk benefit assessments for fish, could be used as a basis for a similar assessment regarding the consumption of whales and seals.

### **Scope**

- The purpose of the FAO/WHO Expert Consultation was to provide a framework for assessing the net health benefits or risks of fish consumption that would assist governments to prepare advice for their own populations.
- Fish was defined as finfish and shellfish, whether of marine or freshwater origin, farmed or wild. Marine mammals and algae, as well as sustainability issues and environmental impacts, although important, were considered to be outside the scope of the Consultation.
- Based on the strength of the evidence, the Consultation examined the benefits of fish consumption on neurodevelopment and prevention of cardiovascular disease. Multiple other possible benefits were reviewed in background papers but not focused upon by the Consultation in their consideration of relative risks and benefits. The Consultation also examined the risks from fish consumption of MeHg and DLCs, including dioxins, furans and dioxin-like PCBs.
- The group was also requested to conduct an analysis of these benefits and associated risks and make a series of recommendations for target populations: including fetuses, infants/young children, women of reproductive age and high fish consumers as well as the general population.

### **Results and Conclusions**

The table below demonstrates the harm from MeHg compared with the benefit from EPA+DHA in terms of the number of IQ points lost or gained by a child as a result of its mother having consumed four servings of fish a week of differing MeHg and EPA+DHA contents. Fish serving size was estimated to be 100 g, DHA:EPA+DHA ratio was assumed to be 0.67 and maternal body weight was assumed to be 60 kg.

The numbers in the upper row in each cell are estimates of IQ points lost from MeHg exposure. The lower value is calculated using a coefficient for the central estimate of -0.18 while the higher value uses the upper bound estimate of -0.7 The dose-response models from which these figures were drawn are from three meta-analyses relating maternal MeHg body burden, expressed as Hg concentrations in maternal hair, to child IQ. Two of the analyses (Axelrad et al, 2007 and Cohen et al, 2005) were based on three major cohort studies conducted in the Faroe Islands, New Zealand, and the Seychelles. These studies included a battery of tests conducted on children aged 7-9 years. A third analysis (Carrington and Bolger, 2000) utilized pooled data on developmental milestones from Iraq and Seychelles on children aged 1-3.

The numbers in the lower row in each cell are estimates of IQ points gained from DHA exposure calculated using a coefficient of 4 IQ points for 100 mg DHA intake. The maximum positive effect from DHA was estimated as 5.8 points (REF).

The same type of table can be constructed to compare the harm from DLC exposure, in terms of increased mortality from cancer (WHO 1998 and IARC 1997), with the benefit of DHA+EPA consumption

Four servings per week

		EPA+DHA			
		< 3 mg/g	3 < 8 mg/g	8 < 15 mg/g	> 15 mg/g
MeHg	≤ 0.1 µg/g	-0.08, - 0.31 3.1	-0.08, - 0.31 5.8	-0.08, - 0.31 5.8	-0.08, - 0.31 5.8
	0.1 ≤ 0.5	-0.48, - 1.9 3.1	-0.48, - 1.9 5.8	-0.48, - 1.9 5.8	-0.48, - 1.9 5.8
	0.5 ≤ 1.0	-1.2, - 4.7 3.1	-1.2, - 4.7 5.8	-1.2, - 4.7 5.8	-1.2, - 4.7 5.8
	> 1.0	-2.4, - 9.3 3.1	-2.4, - 9.3 5.8	-2.4, - 9.3 5.8	-2.4, - 9.3 5.8

\* Assuming DHA ratio 0.67

The main overall conclusions reached by the Experts were:

- Consumption of fish provides energy, protein, and a range of other important nutrients, including the long-chain n-3 poly unsaturated fatty acids (LC n-3 PUFA).
- Eating fish is part of the cultural traditions of many peoples and in some populations is a major source of food and essential nutrients.
- Among the general adult population, consumption of fish, particularly oily fish, lowers the risk of coronary heart disease (CHD) mortality. There is absence of probable or convincing evidence of CHD risks of MeHg. Potential cancer risks of DLCs are well below established CHD benefits.

- When considering benefits of LC *n*-3 PUFA vs. risks of MeHg among women of childbearing age: maternal fish consumption lowers the risk of suboptimal neurodevelopment in their offspring compared to women not eating fish in most circumstances evaluated.
- At levels of maternal DLC intake (from fish and other dietary sources) that do not exceed the provisional tolerable monthly intake (PTMI) of 70 picograms/kg bodyweight/month established by JECFA, neurodevelopmental risk is negligible. At levels of maternal DLC intake (from fish and other dietary sources) that exceed the PTMI, neurodevelopmental risk may no longer be negligible.
- Among infants, young children, and adolescents, the available data are currently insufficient to derive a quantitative framework of health risks and benefits of eating fish. However, healthy dietary patterns that include fish and are established early in life influence dietary habits and health during adult life.

### **Recommendations**

- To minimize risks in target populations, the Consultation recommended a series of steps that member states should take to better assess and manage the risks and benefits of fish consumption and more effectively communicate with their citizens:
  - Acknowledge fish consumption as an important food source of energy, protein, and a range of essential nutrients and part of the cultural traditions of many peoples.
  - Emphasize the benefits of fish consumption on reducing CHD mortality (and CHD mortality risks of not eating fish) for the general adult population.
  - Emphasize the neurodevelopment benefits to offspring of fish consumption by women of childbearing age, particularly pregnant women and nursing mothers, and the neurodevelopment risks to offspring of such women not consuming fish
  - Develop, maintain, and improve existing databases on specific nutrients and contaminants, particularly MeHg and DLCs, in fish consumed in their region.
  - Develop and evaluate risk management and communication strategies that both minimize risks and maximize benefits from eating fish.

## References

**Axelrad, D.A., Bellinger, D.C. Ryan, L.M. & Woodruff, T.J.** 2007 Dose-response relationship of prenatal mercury exposure and IQ: an integrative analysis of epidemiologic data. *Environ Health Perspect.* 115(4):609-15.

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**WHO** 1998. Assessment of the Health Risk of Dioxins: Re-evaluation of the Tolerable Daily Intake (TDI). Geneva: World Health Organization, European Centre for Environment and Health, and International Programme on Chemical Safety

## 2. More to it - benefits from mammals?

Presented by **Edel Oddny Elvevoll**; Professor, Seafood and Nutrition, University of Tromsø

The beneficial health aspects of seafood, including mammals, have primarily been linked to high intakes of marine long chain omega-3 polyunsaturated fatty acids (LC *n-3* PUFA) in particular eicosapentaenoic acid (EPA) (20:5, *n-3*) and docosahexaenoic acid (DHA) (22:6, *n-3*) particularly since the discovery of the low incidence of CVD in Greenland Eskimos. Possible benefits from other substances have been partly neglected even if significant vascular benefits from modest and lean fish consumption have been observed. Recent meta-analyses, assessing the effects of consumption of fish, found that people who ate lean or fatty fish at least once a week had a significantly reduced risk of cardiovascular events.

Seafood is considered to be a valuable source of proteins. Both individual amino acids and the total amino acid profile of fish may differ from those in other food sources. Protein hydrolysates obtained by digestion or enzymatic hydrolysis of various tissues are rich sources of bioactive peptides. A review on peptides, from marine raw materials

shows that they possess various biological activities such as: blood pressure attenuation, antioxidation, immune system modulation, regulation of cell proliferation and are anti-anaemic.

LC *n-3* PUFA are highly susceptible to oxidation. Peptides exhibiting antioxidative capacity (AOC) have been shown to be encrypted in seafood muscle proteins. Such components may protect the fatty acids during digestion and uptake as well as exhibit antioxidative effects in general.

Additional aspects of the Eskimo diet, in associations to development of CVD, such as the effects of traditional food habits including extensive consumption of visceral organs and the consumption of less processed food items has still to be explored. Eating practices that manages to maintain traditional food habits with extensive consumption of visceral organs may be beneficial for preventing atherosclerosis and hypertension. Visceral organs (liver, heart, kidney, gonads) are known as rich sources biological active molecules. The main task of modern food processing is to ensure tasty, edible and stable products. Processing and household preparation caused huge losses of water soluble compounds like taurine (30-80%). Seafood, and especially invertebrates such as molluscs and crustaceans, are high in taurine (2-aminoethanesulfonic acid).

A randomized and parallel intervention trial was designed to evaluate effects of both *n-3* PUFA and taurine. An enhancement of HDL-cholesterol and reductions in LDL-cholesterol, total cholesterol and apolipoprotein B were observed in the *n-3* and taurine group but not in the group receiving only *n-3*.

We conclude that *n-3* PUFA intake cannot replace consumption of seafood.

### **3. Impact of marine *n-3* fatty acids in pregnancy on risk of preterm birth, and on risk of asthma and allergies and cognitive development in the offspring**

Presented by **Sjúrður F. Olsen**; Professor, Statens Serum Institut, Dept. of Epidemiology Research, Copenhagen

#### **Risk of preterm birth**

##### *Danish Nutrition Council*

The basis for the recommendations from the National Board of Health, the Danish Veterinary and Food Administration and the latest scientific literature on nutrition during pregnancy has been examined and evaluated, respectively, by the Danish Nutrition Council. Recommendations on weight control, folic acid, iron and calcium, multi-vitamin mineral supplementations and avoidance of alcohol, coffee, and polluted fish are given to mother to be and pregnant women (Olsen *et al.* 2005).

*Nordic Nutrition Recommendations*

The work comprised systematic literature reviews of existing scientific evidence for a balanced diet, a healthy lifestyle, good health, optimal nutrition and avoidance of lifestyle related diseases such as cardiovascular disease, osteoporosis, certain types of cancer, diabetes 2 and related risk factors (Nord 2004:13).

*Birth weight and PUFA*

The average birth weight of 10132 liveborn infants delivered in the Faroe Islands during the period 1969-81 was 3610 g, and is the highest birth weight among 33 geographically defined populations from all over the world. Environmental and genetic factors are discussed (Olsen 1985). When compared with Danish data the Faroese birth weights exceed by approximately 200 g and the gestation was 4 days longer. Half of birth weight difference (roughly 100 g) is explainable by the longer gestation. The foetal growth rate is also higher. The intake of n-3 PUFA in the Faroese exceeds that in Denmark by far. High amounts of dietary n-3 PUFA may prolong gestations in humans by interfering with uterine production of prostaglandins, possibly inhibiting production of PGF2 alpha and PGE2, which are mediators of uterine contractions and cervical ripening (Olsen *et al.* 1986).

*Pre-term delivery*

A randomised controlled trial on pregnancy duration with 533 healthy Danish women participating showed that fish-oil supplementation in the third semester prolongs the pregnancy without detrimental effects on the growth of the foetus or on the course of labour (Olsen *et al.* 1992). Moreover, an even larger randomised clinical trial comprising 19 hospitals in Europe and 1619 pregnant women revealed that fish-oil supplementation reduced the recurrence risk of pre-term delivery, had no effect on pre-term delivery in twin pregnancies and no effect on intrauterine growth retardation and pregnancy induced hypertension (Olsen *et al.* 2000). These outcomes are partly supported by a large cohort study (8729 pregnant women) confirming that low consumption of fish is a strong risk factor for preterm delivery and low birth weight in Danish women (Olsen SF, Secher NJ 2002). Four recent reviews (Makrides *et al.* 2006; Jensen 2006; Szajewska *et al.* 2006; Horvath *et al.* 2007) on marine n-3 fatty acids and preterm delivery substantiate some of the mentioned outcomes by concluding that marine n-3 fatty acids prolong pregnancy, but this effect may not be clinically important.

*DHA and postpartum depression*

Despite international recommendations that pregnant women increase their DHA intakes a double-blind, multicentre, randomized controlled trial (DHA to Optimize Mother Infant Outcome trial) concluded that the use of DHA-rich fish oil capsules compared with vegetable oil capsules during pregnancy did not result in lower levels of postpartum depression in mothers or improved cognitive and language development in their offspring during early childhood (Makrides *et al.* 2010).

### **Risk of asthma and allergies**

The prevalence of asthma and allergic disease has increased substantially since 1960. The most recent evidence indicates that maternal diet during pregnancy may be particularly important in the development of childhood asthma (Devereux 2006). This seems to be true for fish as food, because frequent intake of fish during pregnancy protects against development of atopy sensitization in the offspring of mothers without atopic disease (Calvani *et al.* 2006). Furthermore, the German cohort study, LISA found that intake of allergenic foods and foods rich in n-6 PUFA during pregnancy may increase and food rich in n-3 PUFA may decrease the risk of allergic diseases in the offspring (Sausenthaler *et al.* 2007). For all types of asthma, allergic asthma, allergic rhinitis and atopic dermatitis the 16 year registry based follow up of the fish oil randomized controlled trial in Aarhus 1990 showed a clear survival probability reduction in the olive-oil group compared to the fish-oil group; the hazard rate of asthma was reduced by 63%, whereas the hazard rate of allergic asthma was reduced by 87% in the fish oil compared with the olive oil group (Olsen *et al.* 2008). However, the findings of Newson *et al.* 2004 does not support these outcomes, since they conclude it seems unlikely that foetal exposure to n-6 and n-3 fatty acids is an important determinant of early childhood wheezing and atopic disease.

#### *Marine n-3 PUFA and leukotriene, thromboxane and prostacyclin production*

Prescott *et al.* 2007 found that neutrophil LTB<sub>4</sub> (proinflammatory) production was significantly reduced in neonates whose allergic mothers had received fish oil while pregnant. Interleukin 6 (IL-6) production was also lowered. And LTB<sub>5</sub> (anti-inflammatory) levels were positively correlated with n-3 PUFA membrane levels. Prescott *et al.* 2007 conclude that maternal dietary changes can modify neonatal neutrophil function and thereby have implications for the early immune programming. Sørensen *et al.* 1993 discovered that fish oil administered to pregnant women was metabolized to the eicosapentaenoic acid-derived eicosanoids thromboxane A<sub>3</sub> and prostacyclin I<sub>3</sub>, and as a consequence, the analog products of arachidonic acid tended to be lowered. Whether these biochemical effects will prove beneficial in the prevention or treatment of pre-eclampsia and uterine growth retardation remains to be seen.

### **Cognitive development in the offspring**

The rationale behind the positive impact on offspring's neurodevelopment due to maternal intake of DHA is based on the following three facts: 1) DHA has been shown to be essential to neurodevelopment in very prematurely born children, 2) DHA is the most abundant fatty acid in the brain, and 3) a substantial accretion of DHA take place in the third trimester of pregnancy.

#### *PUFA and IQ*

This rationale was supported by an IQ-study (Helland *et al.* 2003) showing that children's mental processing scores at 4 years of age correlated significantly with maternal intake of DHA and EPA during pregnancy. The group concluded that maternal intake of very-long-chain n-3 PUFAs during pregnancy and lactation may be favourable for later mental

development of children. This study was followed up three years later by a randomized double-blinded investigation concluding that maternal plasma phospholipid concentrations of alpha-linolenic acid and docosahexaenoic acid during pregnancy were correlated to sequential processing at 7 years of age. No significant effect of n-3 fatty acid intervention on total IQ was observed (Helland *et al.* 2008). A similar study of maternal seafood consumption in pregnancy and neurodevelopmental outcomes of children from age 6 months to 8 years showed that low maternal seafood intake was associated with increased risk of suboptimum outcomes for prosocial behaviour, fine motor coordination, communication, and social development scores (Hibbeln *et al.* 2007). These results were corroborated by a prospective population-based cohort study of pregnant women and 25446 children showing that maternal fish intake during pregnancy and the duration of breastfeeding are independently associated with better early child development (Oken *et al.* 2008).

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#### **4. Food insecurity: the other dimension of risk-benefit considerations in the Canadian Arctic**

Presented by **Grace Egeland**; Associate Professor, McGill University, Center for Indigenous Peoples' Nutrition and Environment and School of Dietetics and Human Nutrition, Macdonald Campus, Ste. Anne de Bellevue, Quebec, Canada

Contaminant risks in Arctic communities need to be considered in the light of benefits in a risk management approach. Benefits include socio-cultural cohesion, self-sufficiency and self-determination, as well as nutrient benefits. However, when exactly do risks outweigh benefits is an area of discourse that has and will continue to be an source of debate and contention. In public health, judgment should prevail especially when holistic quantitative assessments are not feasible. One public health analogy that may serve as useful is that in developed countries, HIV-infected mothers are discouraged from breastfeeding to prevent HIV transmission to offspring. However, in many developing countries, HIV-infected mothers are encouraged to exclusively breastfeed for the first 4-6 months given the prevailing risks of early mortality due to unsafe bottle feeding. Perhaps

this analogy could be useful in promoting greater tolerance among diverse health and environmental health practitioners for respecting a range of risk management solutions to contaminant exposures. Too often the debate becomes polarized because the opposite and extreme ends of the political spectrum on environmental issues both view a tolerance of alternative approaches to risk management as an indication that environmental contaminants are not being taken seriously and that the risk assessment process could then be viewed as faulty. We need to move beyond this polarized, contentious and simplistic thinking on environmental issues.

In the context of Arctic Indigenous Peoples health, public health authorities in partnership with Indigenous Peoples' organizations need to evaluate a broad range of issues. These include the now recognized association of disenfranchisement from land and culture as a leading health determinant, and where traditional food harvesting, sharing, and community feasts provide an important context of social cohesion. Further, throughout the Circumpolar North, there are few opportunities for engagement in paid labour activities with resulting economic hardship and food insecurity. Among 16 communities surveyed as part of the Nunavut Inuit Child Health survey, 69.6% of households with preschoolers aged 3-5 years were food insecure and 56% were child food insecure (Egeland *et al.*, 2010). Children residing in food insecure homes were more likely to have consumed traditional food and less likely to have consumed milk during the previous day. Further, children from food insecure homes consumed more sugary drinks and had a lower healthy eating index scores. Furthermore there was a borderline interaction in terms of traditional food and food security status, as preschoolers who were both food insecure and consumed no traditional food in the past day had a higher prevalence of anemia (Egeland *et al.*, 2011a).

Likewise, in the 36 Arctic communities assessed in the International Polar Year Inuit Health Survey, the prevalence of food insecurity was 62.6% (Egeland *et al.*, 2011b). We found that both food insecurity and the nutrition transition represented a dual burden on nutrient intakes. For example, red blood cell (RBC) trans-fatty acids was higher among adults from food insecure households when compared to those from food secure households, whereas serum 25(OH)D (a marker of vitamin D status), RBC n-3 fatty acids, and serum ferritin (a marker of iron status) was significantly higher among those consuming traditional food in the past day. Nutrient intakes also varied by food insecurity and previous day traditional food intake indicating that these two factors are contributing to a multifaceted shift in diet quality in Canadian Arctic communities. As food insecurity and nutrition transition were associated with differences in dietary quality early in life among the preschoolers and also among the adults, the emerging concern is that the stressors associated with food insecurity and nutrition transition will, over the life-course, have an impact upon nutritional health with implications for increased risk of diet-sensitive chronic diseases. Further, our research indicates that even small amounts of traditional food consumption can contribute greatly to improved nutrient exposures (Johnson-Down and Egeland 2010).

It is against the backdrop of these specific findings and the broader social determinants of health that speak to the importance of promoting traditional food consumption in Arctic

communities. The IPY Inuit Health Survey team is currently evaluating contaminant exposure levels and working through communication strategies that can promote traditional food for the majority, while minimizing contaminant exposures for the minority of very high-end consumers. It is a difficult process to navigate and one that is riddled with complexities. However, one helpful area for public health practitioners and Indigenous Peoples' representatives is the safety factor which is now referred to as the uncertainty factor which is applied uniformly in the methyl-mercury risk assessment process. When biomonitoring of contaminant exposures is directly available for a population we have less uncertainty regarding the range of contaminant exposures occurring. Thus, many health practitioners believe that in these situations we can directly utilize the NOEL (no-observed-effect level) available from population-based studies when assessing risk and management approaches. By utilizing the NOEL, we are enabled to promote traditional food consumption to a greater degree with a reasonable certainty of negligible contaminant risks.

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## 5. Risk versus benefits of pilot whale consumption

Presented by **Pál Weihe**; Physician, Researcher, Department of Occupational Medicine and Public Health, Faroe Islands

There are many accounts of the importance of the pilot whale for the Faroese people. If some years went by without any whales, it was reflected in the household, and the joy was great, when this gift from God again appeared from the sea. There is no doubt that this food source in many ways has contributed to good health and has remedied imminent

hunger in many homes (Joensen 2009). As late as in the 1970s, school doctors would write on the note for the parents that they should make sure that blubber was included with the breakfast.

In 1977 the first examinations were carried out to document the contamination of the meat, blubber, liver and kidneys of pilot whales. They showed that the mercury concentration in the meat itself was high, and that it was further increased by about 100-fold in the liver and kidneys, as compared to the whale meat. This led to the first advice from the Chief Medical Officer of the Faroes to the general population to limit the consumption to only one main meal weekly and avoid liver and kidneys (Chief Medical Officer 1997). Since 1980, pregnant women have been advised to limit their consumption of pilot whale meat and blubber.

Several birth cohorts have been established in the Faroes in order to discover the health effects related to mercury and organochlorine exposure:

**Cohort 1:** A cohort of 1022 singleton births was assembled in the Faroe Islands during a 21-month period of 1986-1987. The children have been examined at age 7, 14 and 23 years of age. Effects on brain function associated with prenatal methylmercury exposure appeared widespread (Grandjean *et al* 1997).

**Cohort 2:** The findings from Cohort 1 suggested that exposure assessment should encompass several lipophilic pollutants in addition to methylmercury. As a follow-up, Cohort 2 was therefore established during a 12-month period in 1994-1995 and included 182 singleton term births from consecutive births at the National Hospital in Tórshavn, Faroe Islands. Relevant obstetric data were obtained by standardized procedures and supplemented by a brief nutrition questionnaire. These children were first examined by the Neurological Optimality Score at age two weeks (adjusted for gestational age), and then again at 7 months of age. Subsequent examinations were at age 18 months and then at 12 month intervals up to age 120 months. At 42 months, a comprehensive medical examination with the Neurological Optimality Score was included. For comparison with Cohort 1, detailed neurobehavioral tests were carried out at age 7 and 10 years.

**Cohort 3:** New insight into health risks caused by environmental pollutants and changing exposure patterns in the Faroes lead to the formation of Cohort 3 from consecutive births at the main hospital in the capital Tórshavn between 1 April, 1998 and 29 February, 2000. Because of dietary recommendations from the Faroese health authorities, methylmercury exposures had now decreased, thus allowing better characterization of possible effects of PCBs and other lipophilic contaminants. Cohort 3 consists of 547 children. Nutritional habits were recorded by questionnaire (number of whale meat dinners per month during pregnancy and before pregnancy; number of fish dinners per week; ingestion of blubber with whale meat or fish). A subgroup of Cohort children was examined with regard to immunological parameters at ages 11 and 18 months. The first comprehensive medical examination was carried out just before the booster vaccination at age 5 years, with a follow-up blood sample one month after vaccination. The children were again examined at age 7 years.

Cohort 4: In order to estimate the effect of the dietary recommendations given in 1998, pregnant women in the third trimester of pregnancy were invited to participate in a dietary survey. In total 148 women participated from Oct. 2000 to Sep. 2001. To cover the daily variation a 24 hour recall questionnaire was used on three different days. Food diaries, where all food consumed during one day were reported in total 732 times. To adjust for seasonal variation the women answered a food frequency questionnaire covering the last 12 months with special emphasis on traditional Faroese food items. Blood samples were analyzed for mercury and organochlorines.

Cohort 5: Due to the fact that the contaminant exposure has changed greatly over the last two decades a new birth cohort of 490 children was established from Oct. 2007 to April 2009. It was anticipated that the dietary warnings to pregnant women and not the contaminant concentrations in pilot whale meat and blubber had led to a significant reduction in methylmercury in the blood of pregnant women, however, without a simultaneous reduction in the concentrations of organochlorines. The children were examined by a paediatrician at the age of 2 weeks and 18 months with special emphasis on the central nervous system and the immune system. Blood samples were collected to be analyzed for contaminants and vaccination antibodies, since previous studies in the Faroes have indicated an effect on the immune system by POPs.

The results of the above mentioned studies together with studies on the adult populations have revealed an even gloomier picture of the adverse health effects that are caused by contaminants in pilot whale meat and blubber.

In short the results have so far shown that:

- Mercury from pilot whale meat adversely affects the fetal development of the nervous system (Grandjean *et al*, 1997)
- The mercury effect is still detectable during adolescence (Debes *et al*, 2006, Murata *et al*, 2004)
- The mercury from the maternal diet affects the blood pressure of the children (Sørensen *et al*, 1999)
- The contaminants of the blubber adversely affect the immune system so that the children react more poorly to immunizations (Heilman *et al*, 2006, Heilman *et al*, 2010 and Grandjean *et al*, 2010)
- Contaminants in pilot whales appear to increase the risk of developing Parkinson's disease in those who often eat pilot whale (Petersen *et al*, 2008)
- The risk of hypertension and arteriosclerosis of the carotid arteries is increased in adults who have an increased exposure to mercury (Choi *et al*, 2009 )
- Septuagenarians with type 2 diabetes or impaired fasting glycemia tended to have higher PCB concentrations and higher past intake of traditional foods, especially during childhood and adolescence. Impaired insulin secretion appears to constitute an important part of the type 2 diabetes pathogenesis associated with exposure to persistent lipophilic food contaminants (Grandjean *et al*, 2011)

Currently, studies are underway to examine the fertility of the population since suspicion has been raised that reproductive functions may be decreased because of contaminants in pilot whale meat and blubber.

Mercury in the oceans has been augmented, for instance polar bears now have a hair-mercury-concentration that is about 10-fold greater than during earlier times. PCBs have been added as an environmental toxicant in the second part of the 1900s, but even after bans about 1980 the concentrations in pilot whale have not yet decreased much. In addition, new compounds such as the organic fluorine compounds that are used for textile impregnation and other purposes are now found in increased concentrations in the blood in children, who eat pilot whale (Weihe *et al*, 2008).

The Faroese body burden of pollutants is high when seen in an international perspective (National Research Council 2000). However, the most recent studies have shown that pregnant women eat much less pilot whale meat and blubber than before. This change has resulted in a significant decrease in mercury and POP concentration in the blood of pregnant women.

Based on the latest research results in human populations in the Faeroes the First Medical Officer and the author in 2008 recommend that pilot whale is no longer used for human consumption (Chief Medical Officer 2008) – according to the precautionary principle expressed in the Faroese Statement (Grandjean *et al*, 2008).

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## 5. Environmental contaminants in pilot whales in the NE Atlantic

Presented by **Maria Dam**; Dr. Scient. Head of Department of Environment Agency

In the 1970's the presence of high concentrations of mercury and persistent organic pollutants like PCB's and DDT in pilot whales, taken in the traditional whale hunt in the Faroe Islands, became apparent (Reinert, 1976). Also, some analyses on abdominal lipid tissue from autopsies at the hospital in the Faroe Islands indicated a population exposed to POPs (Kraul *et al.* 1977). Also analyses of mercury in human hair samples had been initiated<sup>2</sup>. These findings provided the background for dietary advice to limit the intake of pilot whale meat to once a week (Landsdjóralæknin og Landslæknin 1977). Since then, analyses of pilot whale tissue has been done as part of a large ecological pilot whale study (Bloch *et al.* 1993) in 1986-1988 comprising thousands of pilot whales taken in connection with the traditional drive kill in the Faroe Islands in this period. Monitoring of pollutants in pilot whale tissue in the Faroe Islands as a regularly repeated exercise began in 1995 at the Food-, Veterinary- and Environmental Agency.

The relative occurrence of a selection of contaminants is elucidated by the following "ranking list". The list describes the level of pollutants that may be encountered in young pilot whales:

PCB, DDT:	10 000 ng/g lw blubber
Toxaphene:	8 000 ng/g lw blubber
Chlordanes:	4 000 ng/g lw blubber
Mercury:	1 000 ng/g ww muscle
PBDE group:	1 000 ng/g lw blubber
PFC group:	500 ng/g ww liver

Given the phasing out (by regulation) that has taken place, or is to be implemented by agreements under the auspices of the Stockholm convention, for the organic compounds on the list, it is to be expected that the levels at least for the PCB's and pesticides mentioned will decrease rather than increase in the coming years. Also PDBE and eventually also PFCs may be expected to decrease following regulations and /or voluntary reductions in applications, which have been in effect for the last 5-10 years.

The overall mercury concentration in pilot whale meat has been estimated to be 2 mg/kg based on monitoring of mercury in a large number of pilot whales and consideration of

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<sup>2</sup> Bloch *et al.* 1987 reports on results of analyses of hair samples from 151 humans, in which the average mercury concentration was found to be 5.23 ppm.

changes of mercury concentration with whale age and the normal distribution of young and adult females and males in a school of pilot whales.

An assessment of the diets of pregnant women was undertaken in a study in 2000/2001. In combination with monitoring results this enabled estimation of mercury intake from various food items (Dam, 2010 not published). The estimate revealed that even a modest intake of 1.5 g of pilot whale meat per day was still sufficient to make up the largest single food type contribution to the calculated daily sum exposure. Fish, at an intake of 30 g/day, was the food group which provided the second largest mercury exposure for these pregnant women. A similar assessment of PCB exposure gave pilot whale blubber intake at 1.5 gram per day as the largest contributor to the daily PCB intake, with seabirds (here as young or fledging fulmars) with a 2.5 g daily intake as the second largest food PCB source. Similar results were found for PBDEs (Dam and Hoydal, 2008), but then with pilot whale blubber providing the largest intake of PBDE and pilot whale muscle providing the next highest dose.

During the years from 1986 and onwards more than 1100 pilot whales have been analysed for PCB and DDT (or DDE) and mercury. The range of contaminants analysed and found in tissues from pilot whales make it tempting to utter "show me a piece of pilot whale blubber and I'll show you any conceivable contaminant." However, the information on nutrients and overall nutritional value from pilot whale dinners has hardly been described at all, and with the possible exception of fatty acids, nutrients in pilot whales are very poorly known. Though, selenium is monitored as part of the environmental contaminants monitoring in the Arctic and assessment programme (Hoydal and Dam, 2009).

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## 6. Omega-3 long-chain PUFA in health and disease

Presented by **Guðrún V. Skúladóttir**; Professor, Faculty of Medicine, School of Health Sciences, University of Iceland, Reykjavik,

Iceland has been a community with traditional fish and cod liver oil consumption, which had led to relatively high levels of circulating omega-3 long-chain polyunsaturated fatty acids (LC-PUFA) in Icelanders compared to many other populations. In Iceland it has been a customary to supplement ewes diet with fish meal, herring or fish oil in December, during the breeding season and prior to the lambing in the spring. Unpublished data have shown that when ewes were fed 80 g fish meal per day during gestation there was a positive correlation found between the levels of the most unsaturated omega-3 LC-PUFA, DHA, in total lipids of new-born lamb muscle and DHA in maternal circulation (from GV Skuladottir laboratory). In the Icelanders age-related differences were found in plasma phospholipid fatty acids due to changes in dietary patterns (Skúladóttir *et al.*). The results indicated that the elderly tended to eat more of the traditional Icelandic high-fat lamb meat, with relatively high levels of saturated fatty acids and omega-3 LC-PUFA, but they also consumed cod liver oil more frequently. Results from a recent study are in accordance with those of the earlier study, where older heart disease patients reported more frequent use of cod liver oil supplementation and fish consumption than the younger ones (Skuladottir *et al.* 2011)

### Omega-3 LC-PUFA and atherosclerotic disease

In the late eighties crude mortality from ischemic heart diseases was higher among Manitoban residents of pure Icelandic descent than among the Icelandic population. It was found that the relatively high plasma levels of omega-3 LC-PUFA in the Icelanders (around 6% of total fatty acids) reflected the dietary intake of these fatty acids found in the traditional Icelandic diet, fish, fish oil and Icelandic lamb (Skúladóttir *et al.* 1995). Moreover, it was observed that the levels of omega-3 LC-PUFA were higher in the older generation who tended to eat more of the traditional Icelandic diet than the younger ones. On the other hand, the relatively low levels of omega-3 LC-PUFA in the Icelandic-Canadians (around 2% of total fatty acids) reflected the dietary intake of fatty acids originating from grains, fruits and vegetables. In addition, the plasma levels of omega-3 LC-PUFA indicated that the dietary habits of Icelandic-Canadians were rather stable through the generations.

Conclusion: The results from this study supported the idea that omega-3 LC-PUFA, such as Icelanders obtain through their consumption of fish, fish oil, and Icelandic lamb, can afford protection from atherosclerotic disease, even in the face of a diet that in other respects may be counted as atherogenic.

### **Omega-3 LC-PUFA consumption early in pregnancy, mother's health and birth Outcome**

A community with traditional fish and cod liver oil consumption gives an opportunity to study the contribution of cod liver oil (i.e. omega-3 LC-PUFA) consumption to important health aspects for mother and newborn infant. An observational study was performed on healthy and low-risk pregnant Icelandic women, who attended a routine first visit 1999-2001. The pregnant women attended between 11 and 15 weeks and between 34 and 37 weeks of gestation and at each time point filled in food frequency questionnaires for the previous three months. Fourteen percent of the study population (n=436) used liquid cod liver oil in early pregnancy, and this maternal intake was found to be positively correlated with birthweight after adjustment for gestational age at birth and other confounding factors (Olafsdottir *et al.* 2005). Moreover, in the same study group high maternal consumption of omega-3 LC-PUFA in early pregnancy was related to hypertensive disorders in pregnancy (Olafsdottir *et al.* 2006). Cod liver oil is also a good source of vitamins A, D and E, besides being a rich source of omega-3 LC-PUFA. The study showed that there was an increased likelihood of hypertensive disorders in pregnancy with higher intake of vitamin D. However, the results indicate that large amounts of omega-3 LC-PUFA rather than vitamin D are associated with the effect on blood pressure and related disorders in pregnancy.

Conclusions: For healthy Icelandic women without pregnancy complications, regular intake of liquid cod liver oil early in pregnancy is to be considered as positive for the infants health, since higher birthweight has been associated with a lower risk of diseases later in life (Olafsdottir *et al.* 2005). On the other hand, high doses of omega-3 LC-PUFA in early pregnancy, or other nutrients found in liquid cod liver oil, may increase the risk of developing hypertensive disorders in pregnancy (Olafsdottir *et al.* 2006).

### **Omega-3 LC-PUFA and risk of postoperative atrial fibrillation**

Atrial fibrillation is the most common cardiac arrhythmia, and frequently occurs as a complication of cardiac surgery, i.e. postoperative atrial fibrillation (POAF). Evidence links POAF with inflammation, and it has been postulated that the antiarrhythmic and anti-inflammatory effects of omega-3 LC-PUFA may decrease the risk of POAF following open heart surgery. POAF increases the risk of stroke, heart failure, mortality, length of hospital stay and healthcare costs. There is also increasing evidence linking POAF from surgical trauma with systemic inflammation. However the mechanism underlying the pathophysiology of POAF is not precisely known and therefore POAF is challenging to treat, prevent and cure.

Two studies have shown that omega-3 LC-PUFA treatment has beneficial effects for the prevention of atrial fibrillation after coronary artery bypass graft (CABG) surgery. An Italian study (Calo *et al.* 2005) showed that the incidence of POAF in patients supplemented with capsules containing EPA and DHA as ethyl esters for at least 5 days before surgery was 15% compared with 33% in the control group. A German study (Heidt *et al.* 2009) showed that the incidence of POAF in patients who received an intravenous infusion of EPA and DHA as an emulsion of highly refined fish oil, at least 12 hours preoperatively and immediately following surgery was 17.3% compared with 30.6%, in the control group. These two studies were not blinded placebo-controlled studies. Two recent studies found no benefit of short-term fish oil supplementation on the risk of AF following CABG surgery: a British study performed by Saravanan *et al.* 2010) and an Icelandic study performed by Heidarsdottir *et al.* 2010). Both these studies were blinded placebo-controlled studies. In neither of the studies performed in Italy or Germany, were the blood levels of the EPA and DHA assessed, but both studies were conducted in populations that have been reported to have low baseline levels of EPA and DHA in plasma phospholipids (Abbatecola *et al.* 2009; Crowe *et al.* 2008). On the other hand, the baseline levels of the omega-3 LC-PUFA in plasma phospholipids were considerably higher in the British (Saravanan *et al.* 2010) and Icelandic patients (Skuladottir *et al.* 2011). Results from the Icelandic study on patients (n=125) undergoing CABG surgery suggests a u-shaped curve for the relationship between the incidence of AF and quartiles of total omega-3 LC PUFA levels in plasma phospholipids.

Conclusions: The Icelandic cohort study suggests that omega-3 LC-PUFA supplements might prevent POAF in CABG patients with very low baseline levels of these fatty acids in plasma phospholipids, but may appear to have no protective effect or be harmful in those with high levels.

Finally, quoting Aristotle; “Moderation in all things”

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## **7. Fish intake and inflammatory markers – gene expression and lipidomics data**

Presented by **Arja Erkkilä**; PhD, Assistant Professor, Institute of Public Health and Clinical Nutrition University of Eastern Finland

### **Effects of fatty and lean fish intake on cardiovascular risk factors**

Intake of fish and long-chain n-3 fatty acids has been of wide interest due to their beneficial effects on cardiovascular risk factors and lowering of coronary heart disease (CHD) risk. We conducted a study to examine the effects of fatty fish and lean (white)

fish on cardiovascular risk factors in subjects with CHD using multiple drugs for this condition.

The study was an 8-week controlled, parallel intervention. Inclusion criteria were myocardial infarction or unstable ischemic attack, age under 70 years, use of betablockers and presence of sinus rhythm. The subjects were randomized to one of the following groups: 4 meals/week fatty fish (n=11), 4 meals/week lean fish (n=12) and control diet including lean meat (n=10).

Compliance to the intervention diets was good as assessed by food records and fish consumption questionnaire. In addition, the proportions of eicosapentaenoic and docosahexaenoic acids in serum lipids increased in the fatty fish group. Systolic and diastolic blood pressure levels decreased in the lean fish group. Serum total triglyceride concentration did not significantly change. HDL cholesterol concentration change differed among groups but without significant post hoc differences. There were some inconsistent changes in circulating levels of inflammatory markers, like reduction in ICAM-1 in the lean fish group. Analysis of serum lipidomics profiles showed that ceramides, lysophosphatidylcholines and diacylglycerols decreased significantly in the fatty fish group, while there were no significant changes in the lean fish or control groups. Serum IL-6 concentrations correlated significantly with plasma ceramides concentration in the baseline.

Our results suggest that lean fish intake at least four times per week could reduce blood pressure levels in CHD patients. Furthermore, fatty fish intake changed lipidomic profile markedly, showing decreases in potential mediators of lipid-induced insulin resistance and inflammation. The results point also that IL-6 could be the link between ceramides and insulin resistance and inflammation.

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## 8. Risk versus benefit of whale and seal consumption in Greenland

Presented by **Gert Mulvad**; Researcher and Family Physician at the Centre for Primary Health Care in Nuuk, Greenland.

The traditional Greenlandic diet is to a large extent based upon marine animals and fish. However, for some generations the modern diet has been a mixture of traditional and imported food. Due to the harsh weather conditions most of the fresh food comes from wild marine mammals, terrestrial animals and fish. Greenland has a production of lamb and a limited supply of vegetables but most fabricated foods are imported from outside. A large part of the diet still stems from seafood, fish or sea animals, but imported foods are expected to provide an increasing part of the energy consumption. In any community it is important how food is produced, how it is prepared and how it is consumed. These things are important to the individual and for the way people socialize. That is why food is more than just “nutrition”, it is also essential for social life and the ways families function. Since the present food supply is increasingly imported; arriving fully, or almost fully fabricated, the quality of nutrition changes. Along with this public health may be affected, as well as the social aspects of eating and preparing meals. Still the traditional diet is very important to the population both culturally and financially. It is also of importance in order to get sufficient nutrients, because in many places the imported food available is mostly of poor quality.

High levels of contaminants transported over a long range to the Arctic have been documented by AMAP 2009. In Greenland high contents of organic contaminants are found in people and the pollution has reached a level of concern. A common problem for some environmental contaminants is that they have half lives of many years. They are also transported a long way from globally remote areas and can cause health problems for generations. The environmentally persistent pollutants (POPs) that have been monitored and examined by the Arctic Monitoring and Assessment Program, (AMAP), includes PCBs, organochlorpesticides such as DDT, HCB, HCH, chlordane, dieldrin and toxaphene, and heavy metals such as lead (Pb), mercury (Hg) and cadmium (Cd). These POPs are bioaccumulated in the marinefood chain in fatty tissue (e.g. PCBs and pesticides) and organs such as liver and kidney (heavy metals), creating the highest levels in orsoq/blubber and organs from seals and tooth whales. Baleen whales, however, have a lower place in the food chain and are therefore less contaminated. The highest levels are also found in the oldest individuals. Humans and polar bears are at the top of the food chain, and are thus highly exposed to these chemicals. Generally the levels are low in fish from Greenland and it is not a problem to eat Greenlandic fish. In the Baltic levels in seals have been found to be up to 100 times higher than along the coasts of Greenland, but in the countries around the Baltic, the seals are not eaten. Currents in the sea and in the air spread the contaminants unevenly so that seals and people along the East coast of Greenland are more exposed to a higher level of most POPs.

In Greenland, research on mercury is extensive. Mercury is a heavy metal that has always been in the environment, it also constitutes pollution without borders. The mercury levels

in blood from Greenlandic people are some of the highest ever measured in human samples. Lead is a well-known contaminant that may stem from hunting bullets or from petrol and gasoline. Cadmium comes mostly from smoking cigarettes. The high smoking frequency in Greenland creates rather high blood levels in Greenlandic people in general. Heavy metals are accumulated on their way through the food chain and are also accumulated in human tissues.

It is not dangerous for adults to eat the traditional food and the change from traditional diets to westernized “McDonaldization” may be a poor option with reference to health. It is with regard to pregnant women, and especially unborn babies, that contaminants cause concern. Clinical studies have shown an effect on the ability to learn and on memory, as a function of exposure to mercury early in life. Some surveys indicate that the hormone balance and the immune system may be affected, and have the potential to interfere with reproduction and the ability to fight infections. Some of these effects may perhaps be counteracted by the fatty acids and antioxidants such as selenium (Se) from sea mammals. As the woman accumulates contaminants throughout her life, contaminants will be present in the body even if the diet is changed during pregnancy. Some surveys also suspect POPs for affecting the quality of sperm.

The traditional Greenlandic diet, where sea mammals are dominant, provides heat, energy and a healthy diet, at least for physically active people; the fat from sea mammals protects against coronary heart disease and possibly also immune and inflammatory diseases. A great amount of evidence from epidemiological studies and clinical trials supports the theory of a protective effect against coronary heart disease for fish consumption and intake of marine n-3 fatty acids. Biological pathways for this risk reduction include membrane stabilization in the cardiac myocyte, inhibition of platelet aggregation, favorable modifications of the lipid profile, decrease in blood pressure and reduction of the inflammatory response of the endothelium. Results from epidemiological studies suggest a threshold effect for the consumption of fish and n-3 fatty acids. Risk reduction is especially important for cardiac sudden death. Nevertheless, protection against non-fatal coronary heart disease has also been observed. That menstrual discomfort in Danish women can be reduced by dietary supplements of seal oil capsules was shown in an intervention study done at Centre of Arctic Environmental Medicine (CAM) at University of Aarhus. Studies indicate that n-3 fatty acid may help preventing preterm births.

Selenium is an important trace element with an antagonistic effect on mercury. A number of vitamins and other trace elements are well represented in the traditional diet, which is a diet high in protein and low in sugar. It is a diet well suited for physically active hunters living in the cold Arctic environment.

Vitamin D is obtained from dietary sources and from endogenous synthesis in the skin. Dietary sources rich in vitamin D are fatty fish and sea mammals. Ordinary meat, milk and eggs contain less vitamin D and vegetables are void of vitamin D. The endogenous synthesis occurs in the skin under ultraviolet light B (UVB) stimulation. The endogenous production depends on sun exposure, age, clothing, skin pigmentation, and use of sun

protection. The exposure to UVB depends again on latitude, solar height, absorption in ozone layer and atmosphere, and reflection from clouds. In Greenland, protective clothing is customary, and summer is short with a low solar zenith altitude. Thus, yearly exposure to UVB -sunlight is limited. However, the traditional Inuit diet is rich in sea mammals that contain large quantities of vitamin D. During the last decades, significant cultural changes have occurred in Greenland. Today, many Greenlanders are living on a westernized Danish diet that is low in natural dietary sources containing e.g. vitamin D. Furthermore, Danish food is not fortified with vitamin D. Thus changes from a traditional- to westernized-fare are associated with a reduced vitamin D status in Greenlanders. A longitudinal study on osteoporosis was conducted in Nuuk, in September 2002. The objective was to evaluate risk factors for osteoporosis and changes in parameters of ultrasound densitometry, after two years, among perimenopausal Inuit women who previously participated in a cross section study. After two years, the prevalence of osteoporosis had doubled. Moreover, this study suggested an association between smoking and change in stiffness and concentration of mono-ortho PCB congeners was strongly and negatively associated with bone stiffness.

Global pollution has reached a level where the environment is affected and there is concern for people and animals on the top of the food chain. Replacement of traditional food by substandard, imported food is a significant concern. Any food recommendation must be structured to the needs of the community and take into consideration the available sources of food. For this reason it is important to keep monitoring the pollution that accumulates in the food chains and to take this information into consideration, together with other available information concerning nutrition. These recommendations have to be well balanced and to incorporate all health aspects of the diet, the social and economic consequences of our diet and how we get the food we need to eat.

### **Recommendation on Greenlandic Foods, from the Greenland Home Rule and the Greenlandic Board of Nutrition and Environment:**

#### **Problems:**

- Change of diet and lifestyle toward westernized food means change in intake of energy, energy giving nutrition, vitamins, minerals and other biologically active substances.
- Simultaneously the significance connection of diet to cultural, occupational and social conditions decreases.
- The Greenlandic food that is at the higher level in the food chain has problems with environmental contamination.
- Incorrect preparation and storage of Greenlandic food can entail risk of foodborne diseases.

#### **Goals:**

- Greenlandic food subjects are included in public institutions' food choices.
- Increased general knowledge about which foods are healthy.

- Increased general knowledge about food hygiene (correct storage and handling).
- Increased general knowledge about preparation methods which foster variation and fulfill culinary and nutritional needs.

### **Recommendations:**

- Follow the 10 food recommendation from the Greenlandic Board of Nutrition and Environment.
- Support local and international initiatives that lower emission of pollutants to the environment.
- Secure infrastructure that promotes the use of Greenlandic foods in homes, retail, institutions and other social settings.
- Inform and educate about food hygiene, storage and preparation of both Greenlandic and imported food.
- Provide guidance and education about how Greenlandic and imported food can be included in one's diet in order to fulfill the nutritional recommendations.
- Support local initiatives that increase food security.
- Pregnant and nursing women can continuously eat varied Greenlandic food, but should be cautious, especially with polar bear, toothed whales, seabirds and old seals. These food subjects can for instance be substituted with low fat fish and land based mammals.
- It is recommended that children and young people follow the same advice as pregnant women. It is recommended to all that they follow the ten dietary advice points devised by the Greenlandic Board of Food Safety.
- Arrange ongoing courses that secure local knowledge on counseling and communication about Nutrition and Health.

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## 9. Health Benefits of Marine Mammal Based Food

Presented by **Hóraldur Joensen**; Faculty of Science and Technology, University of the Faroe Islands

### Whales

In the Faroe Islands whaling is still a part of the traditional, sustainable exploitation of marine resources. Thirteen whale species (cetaceans) migrate through, and some remain, in Faroese waters. These are: blue whale (*Balaenoptera musculus*), fin whale (*Balaenoptera physalus*), sei whale (*Balaenoptera borealis*), minke whale (*Balaenoptera acuturostrata*), humpback whale (*Megaptera novaeangliae*), sperm whale (*Physeter macrocephalus*), northern bottlenose whale (*Hyperoodon ampullatus*), killer whale (*Orcinus orca*), long-finned pilot whale (*Globicephala melas*), white-beaked dolphin (*Lagenorhynchus albirostris*), white-sided dolphin (*Lagenorhynchus acutus*), bottlenose dolphin (*Tursiops truncatus*) and harbour porpoise (*Phocoena phocoena*) (Bloch *et al.* 2000). The non-commercially hunted species these days are first and foremost long finned pilot whale and different sorts of dolphins, like Atlantic white-sided dolphin and bottlenose dolphin. A low and varying number of northern bottlenose whales are also slaughtered annually. The whales are taken by traditional drive fishery (Joensen 2009).

## Seals

Seven seal species (pinnipeds) are observed in waters off the Faroe Islands. These are: hooded seal (*Cystophora cristata*), bearded seal (*Erignathus barbatus*), grey seal (*Halichoerus grypus*), harp seal (*Pagophilus groenlandicus*), ringed seal (*Pusa hispida*), harbour seal (*Phoca vitulina*), Atlantic walrus (*Odobenus rosmarus rosmarus*). The grey seal is the only species which is currently breeding in the Faroe Islands. In former times a breeding stock of harbour seal existed in the Faroes, but due to high hunting pressure the stock collapsed. The last was taken in 1845. Since then only migrating harbour seals are seen in Faroese waters (Bloch *et al.* 2000). Regular and traditional hunting of seals does not occur anymore in the Faroe Islands.

## Fatty acids in blubber of marine mammals

Fatty acid composition of a large number of seal- and whale-blubber samples have been measured lately in the Canadian Arctic. The marine mammals were 80 bearded seals (*Erignathus barbatus*), 33 harbor seals (*Phoca vitulina*), 239 harp seals (*Pagophilus groenlandicus*), 32 hooded seals (*Cystophora cristata*), 281 ringed seals (*Phoca hispida*), 53 walruses (*Odobenus rosmarus rosmarus*), 105 beluga whales (*Delphinapterus leucas*), and 20 narwhales (*Monodon monoceros*). Except for narwhale the blubber of the other species was fairly rich in the healthy long-chain highly unsaturated fatty acids, LC-HUFA (Thiemann & Iverson 2008). Similarly, analysis of white whale (*Delphinapterus leucas*) shows that its blubber is rich in the healthy longchain monounsaturated fatty acids, LC-MUFA, and long-chained polyunsaturated fatty acids, LC-PUFA (Dahl *et al.* 2000).

## Stratification of FA in whale blubber

The relative stratification index of the fatty acid in blubber columns of longfinned pilot whale, Atlantic white-sided dolphin, bottlenose dolphin, and Northern bottlenose whale caught in the Faroe Islands shows that the short-chain saturated fatty acids, SC-SAFA, short-chain monounsaturated fatty acids, SC-MUFA, and short-chainpolyunsaturated fatty acids SC-PUFA are concentrated mainly in the outer layer while the content of long-chain saturated fatty acids LC-SAFA, LC-MUFA and LC-PUFA is higher in the inner layer (Grahl-Nielsen & Joensen, unpublished data). A similar distribution of fatty acids is found in minke whale blubber (Olsen & Grahl-Nielsen 2003).

## Seal meat and blubber

A study evaluating the nutritional composition of blubber and meat of hooded seal (*Cystophora cristata*) and harp seal (*Phagophilus groenlandicus*) from Greenland showed that seal blubber is an excellent source of LC-HUFA like eicosapentaenoic acid, EPA, and docosahexaenoic acids, DHA. Seal meat is rich in minerals and proteins with a well-balanced amino acid composition. The content of trace elements is high, particularly

iron (379 ug/g) and zinc (30 ug/g). The vitamin content is also high especially vitamin A, D3 and B12 (Brunborg *et al.* 2006). The fatty acid composition of seal (*Halichoerus grampus*) and harbour seal (*Phoca vitulina L.*) blubber is significantly different from the animal's diet, probably due to the species specific inherit metabolism (Grahl-Nielsen & Mjaavatten 1991).

### **Nutritients and POPs South African seal**

Chemical analysis of Cape fur seal meat and blubber shows that seal in Southern Africa has a very low burden of persistent organic pollutants (POPs), compared to similar analysis in the North Atlantic, and the contents of minerals, protein, amino acids and polyunsaturated fatty acids meets well the nutritional requirements of humans (Koep *et al.* 2007).

### **B vitamins in whales and seals**

A study of traditional foods, including seals and whales, of Canadian Arctic Indigenous Peoples showed so high levels of folate, pyridoxine, niacin and riboflavin that these foods have the potential to contribute significantly to the vitamin requirements of these boreal peoples (Hidiroglou *et al.* 2008).

### **PUFA from marine mammals is superior**

A comparison of marine mammal fat and fish intake showed that fat of seals and whales is more important than fish for red blood cell n-3 LC-PUFA levels among the Nunavik Inuit, even if daily intake of fish is higher than marine mammal meat and fat (Lucas *et al.* 2010).

### **Vitamin A, D, E in whales and seals**

Sea mammals fats (beluga, narwhale, seal, walrus) have been found to be not only good but excellent sources of vitamins A, D and E, therefore seals, whales and other traditional food resources rich in fat-soluble nutrients are recommended to protect vitamin nutrition in indigenous boreal populations (Kuhnlein *et al.* 2006).

### **PUFA distribution on TAG of seal and fish oil - absorption difference**

The positional distribution of LC-PUFA like EPA, DPA (docosapentaenoic acid), and DHA in the TAG (triacylglycerol) molecules is different in seal blubber oil and in fish oil. Stereospecific analysis of seal blubber oil has revealed that EPA, DPA, and DHA occurred mainly in the sn-1 and sn-3 positions of the TAG molecules. The same analysis of menhaden oil showed that DPA and DHA occurred mainly in sn-2 position, and EPA was equally distributed in the sn-2 and sn-3 position and only sparsely in the sn-1 position (Wanasundara & Shahidi 1997). Since fatty acids in the sn-1 and sn-3 position on the TAG are liberated by regio-specific enzymes like pancreatic lipase, and fatty acids

attached to the sn-2 position of the TAG are supposed to be absorbed and distributed in the body in a less efficient way, the EPA, DPA, and DHA in seal blubber oil might be more effectively absorbed in the body than those in fish oil (menhaden oil) (Wanasundara & Shahidi 1997).

### **LC-HUFA accretion in serum PL**

Daily consumption of 20 g of encapsulated seal oil resulted in a decrease of the n-6/n-3 ratio and the coagulant inhibitor, protein C, and an increase of EPA, DHA, and DPA, EPA/AA, (AA: arachidonic acid) DHA/AA and NEFA (non-esterified fatty acids) in serum phospholipids (Conquer *et al.* 1999).

### **N-3 and N-6 FA and physiological impacts**

N-3 and n-6 fatty acids (FA) can be altered metabolically to eicosanoids, a class of bioactive molecules including leukotrienes, prostaglandins, and thromboxanes. Eicosanoids derived from n-3 fatty acids are mainly anti-inflammatory and inhibit platelet aggregation whereas those biosynthesized from n-6 fatty acids are generally proinflammatory and pro-aggregatory. Dietary intake of long-chain highly unsaturated fatty acids, LC-HUFA are found to be inversely related to inflammatory markers such as C-reactive protein, IL-6, E-selectin, soluble intercellular cell-adhesion molecule 1, ICAM-1, soluble vascular cell adhesion molecule 1, VCAM-1, and soluble tumor necrosis factor alpha receptors. EPA and DHA are also shown to have beneficial influence on ventricular arrhythmias, thrombosis, triglyceride, apolipoprotein B, high-density lipoprotein, adhesion molecule expression in plaque, platelet-derived growth factor, nitric oxide-induced endothelial relaxation and blood pressure reduction (DeFillippis *et al.* 2005 and references therein). Furthermore, LC-HUFA lowers the level of atherosclerosis, has antiarrhythmic effects, reduces incidence of congestive heart failure, increases hepatic fatty acid beta-oxidation, suppresses the level of interleukin-B, and increases the level of adiponectin, which reduces inflammation and improves insulin resistivity, reduces heart rate and left ventricular hypertrophy (Lavie *et al.* 2009 and references therein). A large body of evidence show that intake of EPA or a combination of EPA and DHA is an efficacious adjunctive therapy for several psychiatric disorders, including mood disorders, schizophrenia, and ADHD (Freeman *et al.* 2006). Moreover, EPA and DHA supplementation delays cognitive decline in patients with Alzheimer's disease (Freund-Levi *et al.* 2006). There is a growing body of facts indicating that functional deficiencies or imbalances of n-3 and n-6 HUFA may play a role in dyslexia, dyspraxia, autism and ADHD (Cyhlarova *et al.* 2007 and references therein).

### **N-3 and cancer**

N-3 FA have been shown to have anti-carcinogenic effects while saturated FA and n-6 FA may promote cancer development (Prenner *et al.* 1996).

### **N-6/n -3 ratio increment and consequences**

The n-3 polyunsaturated fatty acids are primarily present in fish, shellfish and marine mammals and are limited in land animals and plants. The current western diet is low in n-3 LC-HUFA, which has resulted in a change of the ratio of n-6 to n-3 intakes from 2 to more than 20 within a century. The negative consequences of this twisted n-6/n -3 ratio is increased thrombogenesis, lowered immune response, increased inflammation and decreased neuronal membrane fluidity, function and therewith deteriorated neurotransmission and signalling (Hooijmans & Kiliaan 2008 and references therein).

### **Marine mammal oil and pain**

In a randomized double blind trial whale and seal oil were administered duodenally to patients with inflammatory bowel disease (IBD) and joint pain. The result was a significant reduction of joint pain, back pain and the indexes of IBD-disease activity for both whale and seal oil. Both of the marine oils improved quality of life (Bjorkkjar *et al.* 2009, Brunborg *et al.* 2008).

### **LC-HUFA and mental health**

PUFAs are important structural constituents of the central nervous system, and their functional role in learning and memory has been well documented. Breast milk, a good DHA source, compared to formula had a better effect on verbal skills, performance skills, and overall IQ of the participating infants; the difference was 8 % to 9 %. During the pregnancy the maternal plasma phospholipid DHA status decreased by some 40 % due to selective mobilisation of DHA for development of brain, retina, eye and heart of the fetus (Shahidi 2004, Shahidi & Finley 2001).

### **LC-HUFA and neurons**

In a neuroregenerative experiment n-3 LC- HUFA, especially DHA, had a marked neurite-promoting effect in neurons not only in immature neurons but also in neurons from adult and aged animals (Robson *et al.* 2010).

### **LC-HUFA and gene expression**

In a nutrigenomic experiment with high-density microarrays used to reveal gene-expression changes in response to different PUFA-enriched diets in rats several genes were up-regulated and others down regulated. The products of the up-regulated genes play major roles in synaptic plasticity, learning (Kitajka *et al.* 2004 and references therein) and energy/lipid metabolism (Deckelbaum *et al.* 2006). The down-regulated

genes code for a long list of inflammatory proteins (Deckelbaum *et al.* 2006). The favourable biological effects of especially EPA and DHA include compositional changes of cell membranes and membrane function, activation or suppression of signaling molecules, direct interaction with DNA and transcription factors, influence on enzyme activities, influence on the trafficking between vesicular endoplasmic reticulum and Golgi apparatus, potential scavenging of reactive oxygen species and thereby protection against neurodegeneration, and finally eicosanoids, which are LC-HUFA metabolites (Deckelbaum *et al.* 2006 and references therein).

### **LC-HUFA, antioxidants and neuroprotection**

Intake of EPA and DHA showed increased antioxidant gene expression, higher glutathione peroxidase (GPx) activity, and thereby protection against excessive reactive oxygen species (ROS) (Kaur *et al.* 2008 and references therein). It is established that DHA reduces cell-associated MeHg and prooxidant response from MeHg in cerebellar astrocytes and neurons and therefore has the potential to offer neuroprotection from MeHg (Kaur *et al.* 2008).

### **Selenium in traditional Greenlandic food**

People in Greenland have always had a high intake of selenium through the traditional food of marine origin. Selenium blood levels were significantly correlated with LC-HUFA. The main Se-sources were whale skin, sea birds, seal meat and organs, and fish. Since a rapid westernization of dietary traditions is taking place in Greenland these days the current copious selenium intake is suspected to diminish to an insufficient level in the near future (Hansen *et al.* 2004).

### **Selenium health benefit value, Se-HBV**

A comprehensive Se-index called Se- health benefit value, Se-HBV, has been created in order to integrate Se-specific nutritional benefits in relation to potential mercury exposure risks.  $Se-HBV = (Se:Hg \text{ molar ratio} \times \text{total Se}) / (Hg:Se \text{ molar ratio} \times \text{total Hg})$  Marine food, which is methyl-Hg-polluted but rich in Se has a high positive Se-HBV. The toxic effects of methyl-Hg polluted diets rich in Se are therefore significantly diminished rather than exacerbated (Raymond & Ralston 2009). Avoiding LC-HUFA and Se may be hazardous for healthy prenatal neurodevelopment. “Children of mothers who avoided fish consumption during pregnancy showed developmental impairments 60 times greater than the worst case impairments associated with the highest pilot whale consumption in the Faroes” (Raymond & Ralston 2009 and references therein).

### **Se-compounds counteract methyl-mercury**

Selenium compounds in animal tissues are Se-cysteine, Se-methionine, selenotrisulfides of cystine, selenate, selenite, and several selenoproteins. Some of the more significant mammalian selenoproteins are glutathione peroxidases (GPx, antioxidant enzymes), iodothyronine deiodinases, selenoprotein P, selenoprotein W, selenophosphatase,

mitochondrial capsule selenoprotein, prostate epithelial selenoprotein, DNA-bound spermatid selenoprotein and 18kDa selenoprotein. Several studies have revealed that Se protects animals against the toxicity of Hg, Cd, Pb, Ag and the neurotoxicity of Hg, Cd, Pb and V (Navarro-Alarcon & Cabrera-Vique 2008 and references therein). The Recommended Dietary Allowance (RDA) and Tolerable Upper Intake Level (UL) for Se for adult is 55 microgram/day and 400 microgram/day, respectively. Intake of selenium up regulates the expression of several genes. The high concentrations of Se compounds in the liver counteracts the toxicity of methyl mercury by demethylation and accumulation as mercuric selenide, HgSe, in the lysosomal fraction of hepatocytes (Ikemoto *et al.* 2004). The absorption mechanism could be a receptor-mediated endocytosis (Renaud *et al.* 1989). Mercury is also concentrated in the kidney (Endo *et al.* 2003). The subsequent excretion of HgSe into the feces goes via the bile duct (Renaud *et al.* 1989). Approximately 95% of the absorbed mercury is excreted in the feces and less than 0.05% in the urine (Endo *et al.* 2003). Human studies (Suzuki *et al.* 1991 and references therein) show biological excretion half times, of tracer dose of MeHg administered, varying between 52 days and 98 days. The average biological half time is longer in males (79 days) than females (71 days). More severe MeHg poisoning exhibited biological half times in the range of 35 days to 289 days (Suzuki *et al.* 1991 and references therein). The half times vary between tissues (Curtis 2001 and references therein). Animal studies (Suzuki *et al.* 1991 and references therein) suggest strongly that the individual differences are genetically based. For an adult Canadian with an average number of 8 dental fillings, amalgams are estimated to contribute 30 to 40 percent of the total mercury exposure of 5 to 6 microgram per day (Curtis 2001 and references therein). Selenium deficiency causes a type of osteoarthritis resulting in enlarged joints, shortened finger, toes, and dwarfism (Navarro-Alarcon & Cabrera-Vique 2008 and references therein).

### **Whale meat rich in protein and Se**

Fresh raw pilot whale meat is richer in protein (24.6 g/100g) than fresh raw salmon, cod, haddock, saith, lamb, beef, pork, fulmar, guillemot, puffin and chicken (Poulsen 1995). Pilot whale meat is also a good Se resource. The concentration of Se in raw fresh cod fillet and raw fresh pilot whale meat is 28 microgram/100g and 185 microgram/100g, respectively (Poulsen 1995). When compared with other food products such as tuna (Burger & Gochfield 2011), other fish species, terrestrial meat (chicken, lamb, beef, pork) and meat products, bread cereals and grains, milk cheese and egg, fruit and vegetables the raw pilot meat excels by its extraordinarily high Se concentration (Poulsen 1995).

### **Transgenerational effects of malnutrition**

Animal studies have revealed transgenerational effects of maternal malnutrition during gestation in F0 on increased obesity in adults, glucose intolerance, and altered cardiovascular function in the F1 and F2 generations (Painter *et al.* 2008 and references therein). Other studies the last two decades have showed that suboptimal nutrition in pregnancy can lead to increased risk of diabetes, hypertension and atherosclerosis developing in the offspring, and that these risk can be heritable (Li *et al.* 2010 and

references therein). Moreover, lifestyle-related and adult onset diseases such as cardiovascular disorders, asthma and schizophrenia are rooted in gestation, lactation and early nutrition (Junien 2006 and references therein). Similarly, a study of the transgenerational effects of prenatal exposure to the Dutch winter famine 1944/45 showed that increased neonatal obesity and poor health late in life was not limited to the F1 generation, but continues in the F2 generation (Painter *et al.* 2008, Matthews & Phillips 2010).

### **Diet induced transgenerational effects and epigenetics**

The topical subject of the transgenerational effects of malnutrition during gestation is particular relevant to rural populations shifting from traditional to western diets. A detailed analysis of the dietary change may elucidate the molecular mechanisms behind the epidemic of diabetes, obesity and cardiovascular diseases (Painter *et al.* 2008). A potential explanation for the modern life-style induced metabolic syndrome could be a nutrient-based effect mediated by an epigenetically changed gene expressions (Li *et al.* 2010). These issues will also be of paramount importance for the coastal populations in the high latitudes, because part of our natural food resource, the marine mammals, is currently so contaminated that we have to change our food tradition radically to a foreign, and in many cases, nutritionally inferior diet. High quality healthy food is essential for genetically predisposed people, like Glycogen Storage Disease 3a (GSD3a) patients. GSD3a involves liver and muscles, and is an autosomal recessive disorder in which deficiency of glycogen debranching enzyme activity leads to accumulation of abnormal glycogen with short outer branch chains. It is supposed that due to the traditional protein-rich food regime people suffering from GSD 3a live longer and better in the Faroe Islands than in any other country worldwide (Weinstein & Minarich 2011). As a consequence, the healthy Faroese protein-rich fare is now being introduced as a remedy for GSD 3a in the USA and other countries instead of the formerly recommended carbohydrates (Weinstein & Minarich 2011). Moreover, several young people from the Faroe Islands suffering from carnitine transporter defect (CTD) have already passed away probably due to replacement of the carnitine rich traditional food with foreign protein poor fares.

### **Importance of whaling in the Faroe Islands**

The average number of pilot whales slaughtered annually from 1900 to 1999, was 956 individuals. This is approximately 500 tons of meat and blubber, and corresponds to roughly 30 % of the total meat production. ([http://en.wikipedia.org/wiki/Whaling\\_in\\_the\\_Faroe\\_Islands](http://en.wikipedia.org/wiki/Whaling_in_the_Faroe_Islands), and references therein). The Faroe Islands is an expensive country in which to live, with the highest rate of taxation in the world. Eight percent of the Faroese population has an equivalent income so low that it is characterized as a Risk of Poverty income, according to EU standards. Moreover, 72% has a yearly equivalent income between 195 and 205 thousand DKK ([www.hagstova.fo](http://www.hagstova.fo)). Due to these low earnings, pilot whaling is of great importance generally, and especially so for the rural population, whose existence is extensively based on a subsistence or barter economy.

### **Decontamination of meat and blubber**

The technology necessary to remove pollutants from blubber and meat is being developed. The development of the pH-shift-filtration method (Nolsøe *et al.* 2011) has partly taken place in the Faroe Islands. The meat could be ground in water, the proteins processed, purified and precipitated by the pH shift procedure followed by pressing and further production of sealstick, whalestick or grindstick, something similar to crabstick. The triglycerides in the blubber could be cold extracted without degradation and gently purified in a short path vacuum distillation plant. Subsequently, the oil could be emulsified in a fish gelatine matrix, as protection against oxidative degradation, and thereupon formed into decontaminated healthy artificial blubber of natural appearance.

### **Faroese Dietary Survey & Food Composition Tables**

No extensive and combined public nutrient and contaminant data-base exists in the Faroe Islands. However, The Environment Agency has started construction of a database on Se and some contaminants ([http://www.us.fo/content/us.fo/gransking/Envofar\\_talva.htm](http://www.us.fo/content/us.fo/gransking/Envofar_talva.htm)). Only three dietary surveys (Gudjonson 1937, Vestergaard & Zachariassen 1987 and Veyhe 2006) have ever been conducted in the country. On the subject of food analysis of fish-fillet and lamb meat, a booklet on nutrients and contaminants in cod (Gregersen & Joensen 2004) and a report on fatty acids in Faroese lamb meat have been published (Jonsdottir *et al.* 2001). Moreover, some results from Faroese, Icelandic, Danish, English, Greenlandic and Swedish food analysis have been compiled in Faroese Food Composition Tables (Poulsen 1995). Finally, the Faroe Islands is a member of the Nordic information and communication network regarding safety of seafood products and utilization of resources from the sea and has delivered some available data to this network ([www.seafoodnet.info](http://www.seafoodnet.info)). Regarding contaminants, several reports are to be found on the homepage of Food, Environmental & Veterinary Agency in Faroe Islands ([www.hfs.fo](http://www.hfs.fo) (ritgerdir)).

### **Future studies of raw and cooked food from marine mammals**

1. Measure protein, fat, lipid-classes, fatty acids, vitamins, macrominerals, trace-minerals, selenium compounds, carnitin, taurine in different species seasonally.
2. Study bioactive peptides in raw and fresh, light to heavily fermented and dry whale and seal meet seasonally.
3. Reveal food-health relations in children, youth, adults and the elderly consuming traditional food prepared from marine mammals.

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## **Appendix 2**

### **AGENDA**

#### **Risks versus Benefits of Whale and Seal Consumption 09:00 – 17:00, Friday 14 January 2011**

09:00 Welcome

Objectives of the meeting:

- 5) To establish the status of the temporary knowledge of the balance between the beneficial and detrimental properties of dietary products from marine mammals in the North Atlantic.
- 6) To evaluate the present information on risk and benefits by using the method developed and used by FAO/WHO Expert Consultation on seafood consumption.
- 7) To recommend the government agencies and the general public on risks and benefits by eating meat and blubber products from marine mammals.
- 8) To decide what kind of studies are still needed to validate the positive and negative health effects.

Rapporteur: Harald Holst

09:10 Presentations (25 min. each)

**Jogeir Toppe**, FAO Fish Products and Industry, Fisheries and Aquaculture Department

**David James**, FAO Fisheries and Aquaculture Department

- *A model for a quantitative risk-benefit assessment of seafood consumption*

**Edel Oddny Elvevoll**, Professor, Seafood and Nutrition, University of Tromsø

- *More to it - benefits from mammals?*

**Sjúrdur F. Olsen**, Professor, Statens Serum Institut, Dept. of Epidemiology Research, Copenhagen

- *Impact of marine n-3 fatty acids in pregnancy on risk of preterm birth, and on risk of asthma and allergies and cognitive development in the offspring*

10:50 – 11:10 Coffee break

**Grace Egeland**; Associate Professor, McGill University, Center for Indigenous Peoples' Nutrition and Environment and School of Dietetics and Human Nutrition, Macdonald Campus, Ste. Anne de Bellevue, Quebec, Canada

- *Food insecurity: the other dimension of risk-benefit considerations in the Canadian Arctic*

**Pál Weihe**; Physician, Researcher, Department of Occupational Medicine and Public Health, Faroe Islands

- *Risk versus benefits of pilot whale consumption*

**Maria Dam**; Dr. Scient. Head of Department of Environment Agency

- *Environmental contaminants in pilot whales in the NE Atlantic*

12:30 – 13:00 Lunch

**Guðrún V. Skúladóttir**; Professor, Faculty of Medicine, School of Health Sciences, University of Iceland, Reykjavik,

- *Omega-3 long-chain PUFA in health and disease*

**Arja Erkkilä**; PhD, Assistant Professor, Institute of Public Health and Clinical Nutrition University of Eastern Finland

- *Fish intake and inflammatory markers – gene expression and lipidomics data*

**Gert Mulvad**; Researcher, Family physician at the Centre for Primary Health Care in Nuuk, Greenland.

- *Risk versus benefit of whale and seal consumption in Greenland*

**Hóraldur Joensen**; University of the Faroe Islands

- *Health Benefits of Marine Mammal Based Food*

*14:40 – 16:45 Discussion*

Questions from the 2010 FAO/WHO Expert Consultation on the Risks and Benefits of Fish Consumption which could be discussed:

1. Is a quantitative risk-benefit approach a realistic goal?
2. What data are needed for a quantitative risk-benefit assessment?
3. Which methodologies and experience already exists on quantitative risk-benefit assessment?
4. What are the methodological strengths and weaknesses of the existing methodologies on quantitative risk-benefit assessment?
5. In which time frame would it be possible to develop an international quantitative risk-benefit assessment?
6. Qualitative risk-benefit assessments already exist - is this approach feasible at international level and would it be acceptable to answer the request by Codex?
7. Can the vulnerable groups of the population be clearly defined?
8. Can the groups of food fish and fishery products be clearly defined with respect to the health risks and health benefits to the consumers?
9. Is the “Appropriate Level of Protection” approach useful in this concept?

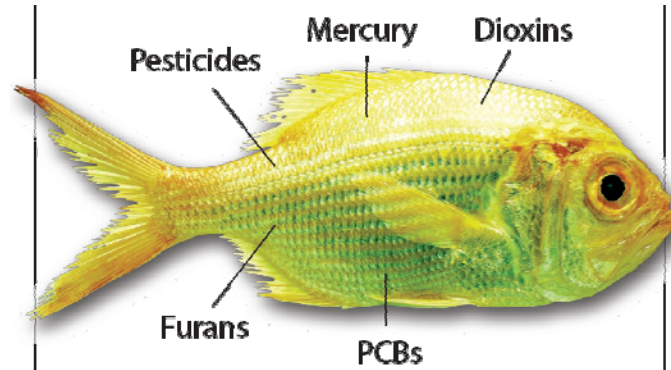
*16:45 – 16:55 Summary of outcomes*

*16:55 – 17:00 Closing remarks*

*17:00 Closing of Risk-Benefit-workshop*

*19:00 Host dinner, socialising, discussion at Madklubben, Bistro-de Luxe, Store Kongensgade 66*

## A Quantitative Model for Risk Benefit Assessment of Seafood Consumption



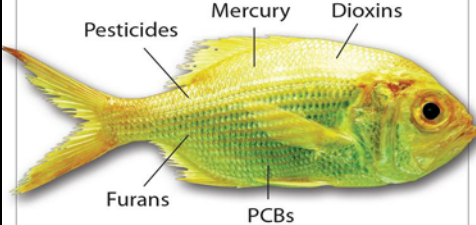
Jogeir Toppe / David James – FAO – January 2011

## Request from Codex Alimentarius

- Growing public concern regarding the presence of chemical contaminants in fish
- Multiple nutritional benefits of including fish in the diet have become increasingly clear



## Brane Fude?



**Mercury is such a potent neurotoxin**  
that even small doses can cause irreversible brain and heart damage. Our single biggest source of mercury exposure is fish consumption.

So why is the federal Dietary Guidelines Advisory Committee—the panel of experts charged with determining what we should eat—getting set to recommend Americans eat 8 to 9 ounces of fish a week, an amount that will put our health at risk?

While it would be easy to chalk this up to politics as usual, too much is at stake. Mercury pollution is placing children and pregnant women at risk as never before. One in six women of childbearing age in the United States has blood mercury levels exceeding the “safe” levels recommended by the EPA.

More than 600,000 babies are born every year at risk of mercury-related birth defects, including mental retardation, learning disabilities, permanent neurological damage, and physical malformations.

In adults, mercury exposure can bring on high blood pressure, cause tremors, and lead to infertility and liver and brain damage.


Mercury is everywhere. In the canned tuna from your local grocery store. In the salmon, shrimp, and shellfish you order at the restaurant. Forty-four states have posted warnings about mercury contamination in their lakes, streams, and rivers.

**Take action.** Go to [www.pcrm.org](http://www.pcrm.org) to send an email to the federal Dietary Guidelines Advisory Committee. Tell them that our health and the health of our children come first. Or write a letter to:

Dr. Janet King  
Chair, Dietary Guidelines Advisory Committee  
Department of Health and Human Services  
200 Independence Avenue, SW, Room 738G  
Washington, DC 20201 Fax: 202-205-0463

**PCRM** P E T A C O N S U M E R F R E E D O M  
WASHINGTON OFFICE PHONE: 202-462-2310

## Brain Washed?



**Did you see this fishy ad last week?**

Animal rights activists are attempting to scare Americans away from some of the healthiest foods on the menu. The American Heart Association says omega-3 fatty acids make fish a must-eat food at least twice a week. But last week the ad pictured at the right implied that all fish are dangerous to eat.

Why would an organization calling itself the “Physicians Committee for Responsible Medicine” (PCRM) run scary anti-fish ads in national newspapers? For starters, PCRM has undeniable connections to People for the Ethical Treatment of Animals (PETA), which has already steered over \$1.3 million to the organization.


Yes, *that* PETA. The animal rights nuts who don’t want us to eat beef, chicken, pork, eggs, dairy foods or fish. No matter what.

PCRM has been publicly rebuked by the American Medical Association for misrepresenting medical science. PCRM’s president is a non-practicing psychiatrist, and also president of the PETA Foundation. And 95 percent of PCRM’s members aren’t doctors at all.

Some PCRM spokespersons endorse violence against people who don’t see the world their way. At a 2003 animal-rights convention, one of them advocated murdering doctors who use animals in their research for cancer and AIDS cures.

Animal rights extremism is felt everywhere. And some of it masquerades as health advice.

Visit [www.ConsumerFreedom.com](http://www.ConsumerFreedom.com) to learn how animal rights activists use junk science, promote violence, and even set up pseudo-medical charities in order to further their crusade. Help this cause by donating online to the nonprofit **Center for Consumer Freedom**.



Don't let the government tell you a fish story.



**TOXIC LEGACY Fishing with caution** October 29, 2007

As many as 600,000 babies may be born in the USA each year with irreversible brain damage because pregnant mothers ate mercury-contaminated fish, the Environmental Protection Agency says. Medical researchers are just beginning to explore such mercury exposure in adults, which can leave some people struggling through life in a disorienting “fish fog.” Nationwide, more than 8,000 lakes, rivers and bays are compromised by mercury’s toxic effects.

Outrageous claim:

*“ 600,000 born annually with brain damage due to fish-eating mothers”*



## Task

- Review data on nutrient and specific chemical (MeHg and DLCs) contaminant levels in a range of fish species
- Review recent scientific literature covering the risks and benefits of fish consumption
- Consider risk-benefit assessments for specific end-points of benefits and risks

## Intention

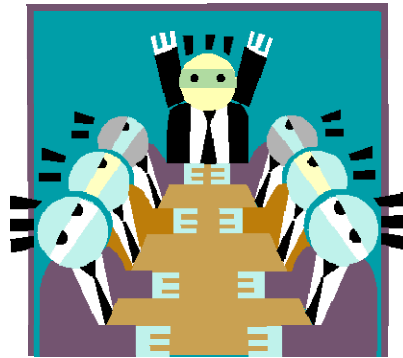
- Provide guidance to national food safety authorities and the Codex Alimentarius Commission on managing risks related to eating fish, taking into account the existing data on the benefits of eating fish

FAO/WHO Expert Consultation on  
the Risks and Benefits of Fish  
Consumption  
25-29 January 2010



## Experts

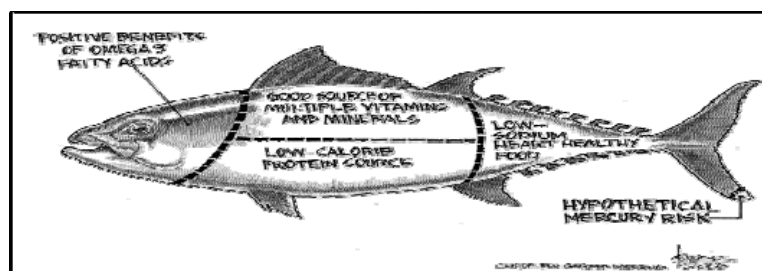
- 17 experts representing 11 countries and 5 continents
- Expertise in nutrition, toxicology, epidemiology, dietary exposure and risk-benefit assessments



## There is convincing evidence that:

- LCn-3PUFA (DHA) is important for optimal brain development during gestation and infancy.
- Maternal fish consumption during gestation and nursing lowers the risk of suboptimal brain development in their children.

- Maternal MeHg intake during gestation increases the risk of suboptimal brain development in their children.
- Based on quantitative risk-benefit analysis of DHA and MeHg, the neurodevelopmental risks of not eating fish exceed the risks of eating fish under most circumstances evaluated.



## MeHg and DHA/EPA

- Decided to conduct a comparison between the effects of prenatal exposure to LC n-3 PUFA and MeHg on child IQ
  - Establish a dose-response relationship from multiple cohort studies
- quantitative risk-benefit analysis

## MeHg Risks

- Three meta-analyses studies
  - Faeroe Islands
  - Seychelles
  - New Zealand
- Assumptions:
  - Serving size 100g
  - Body weight 60 kg
  - Ratio Hg in hair and daily MeHg intake ( $\mu\text{g}/\text{kg}$  body weight/day) is 9.33

## PUFA Benefits

- Four analyses considered
  - Cohen et al. 2005
  - FDA 2010
  - Oken et al. 2008
  - Oken et al. 2008
- Some assumptions:
  - 28 g fish gives 100 mg DHA (average)
  - DHA ratio of LC n-3 PUFA = 0.67

## IQ increase/decrease

- 4 IQ points gain per 100mg/day DHA, maximum gain 5.8 IQ points
- 0.18 (central estimate) to 0.7 (upper limit) IQ points decrease per  $\mu\text{g/g}$  MeHg in maternal hair

One serving per week

		EPA+DHA			
		< 3 mg/g	3 < 8 mg/g	8 < 15 mg/g	> 15 mg/g
MeHg	$\leq 0.1 \mu\text{g/g}$				
	$0.1 \leq 0.5$				
	$0.5 \leq 1.0$				
	$> 1.0$				

\* Assuming DHA ratio 0.67

One serving per week

		EPA+DHA			
		< 3 mg/g	3 < 8 mg/g	8 < 15 mg/g	> 15 mg/g
MeHg	≤ 0.1 µg/g	-0.02, - 0.1	-0.02, - 0.1	-0.02, - 0.1	-0.02, - 0.1
	0.1 ≤ 0.5	-0.12, - 0.5	-0.12, - 0.5	-0.12, - 0.5	-0.12, - 0.5
	0.5 ≤ 1.0	-0.3, - 1.2	-0.3, - 1.2	-0.3, - 1.2	-0.3, - 1.2
	> 1.0	-0.6, - 2.3	-0.6, - 2.3	-0.6, - 2.3	-0.6, - 2.3

\* Assuming DHA ratio 0.67

One serving per week

		EPA+DHA			
		< 3 mg/g	3 < 8 mg/g	8 < 15 mg/g	> 15 mg/g
MeHg	≤ 0.1 µg/g	-0.02, - 0.1 0.77	-0.02, - 0.1 2.11	-0.02, - 0.1 4.4	-0.02, - 0.1 5.8
	0.1 ≤ 0.5	-0.12, - 0.5 0.77	-0.12, - 0.5 2.11	-0.12, - 0.5 4.4	-0.12, - 0.5 5.8
	0.5 ≤ 1.0	-0.3, - 1.2 0.77	-0.3, - 1.2 2.11	-0.3, - 1.2 4.4	-0.3, - 1.2 5.8
	> 1.0	-0.6, - 2.3 0.77	-0.6, - 2.3 2.11	-0.6, - 2.3 4.4	-0.6, - 2.3 5.8

\* Assuming DHA ratio 0.67

One serving per week

		EPA+DHA			
		< 3 mg/g	3 < 8 mg/g	8 < 15 mg/g	> 15 mg/g
MeHg	≤ 0.1 µg/g	-0.02, - 0.1 0.77	-0.02, - 0.1 2.11	-0.02, - 0.1 4.4	-0.02, - 0.1 5.8
	0.1 ≤ 0.5	-0.12, - 0.5 0.77	-0.12, - 0.5 2.11	-0.12, - 0.5 4.4	-0.12, - 0.5 5.8
	0.5 ≤ 1.0	-0.3, - 1.2 0.77	-0.3, - 1.2 2.11	-0.3, - 1.2 4.4	-0.3, - 1.2 5.8
	> 1.0	-0.6, - 2.3 0.77	-0.6, - 2.3 2.11	-0.6, - 2.3 4.4	-0.6, - 2.3 5.8

\* Assuming DHA ratio 0.67

Two servings per week

		EPA+DHA			
		< 3 mg/g	3 < 8 mg/g	8 < 15 mg/g	> 15 mg/g
MeHg	≤ 0.1 µg/g	-0.04, - 0.2 1.5	-0.04, - 0.2 4.2	-0.04, - 0.2 5.8	-0.04, - 0.2 5.8
	0.1 ≤ 0.5	-0.2, - 0.9 1.5	-0.2, - 0.9 4.2	-0.2, - 0.9 5.8	-0.2, - 0.9 5.8
	0.5 ≤ 1.0	-0.6, - 2.3 1.5	-0.6, - 2.3 4.2	-0.6, - 2.3 5.8	-0.6, - 2.3 5.8
	> 1.0	-1.2, - 4.7 1.5	-1.2, - 4.7 4.2	-1.2, - 4.7 5.8	-1.2, - 4.7 5.8

\* Assuming DHA ratio 0.67

Seven servings per week

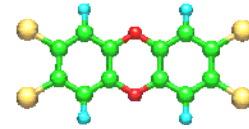
		EPA+DHA			
		< 3 mg/g	3 < 8 mg/g	8 < 15 mg/g	> 15 mg/g
MeHg	≤ 0.1 µg/g	-0.14, - 0.5 5.4	-0.14, - 0.5 5.8	-0.14, - 0.5 5.8	-0.14, - 0.5 5.8
	0.1 ≤ 0.5	-0.84, - 3.3 5.4	-0.84, - 3.3 5.8	-0.84, - 3.3 5.8	-0.84, - 3.3 5.8
	0.5 ≤ 1.0	-2.1, - 8.2 5.4	-2.1, - 8.2 5.8	-2.1, - 8.2 5.8	-2.1, - 8.2 5.8
	> 1.0	-4.2, - 16.3 5.4	-4.2, - 16.3 5.8	-4.2, - 16.3 5.8	-4.2, - 16.3 5.8

\* Assuming DHA ratio 0.67

		EPA+DHA			
		≤ 3 mg/g	3 < x ≤ 8 mg/g	8 < x ≤ 15 mg/g	> 15 mg/g
Hg	≤ 0.1 µg/g	<b>FISH:</b> Butterfish; Catfish; Cod, Atlantic; Cod, Pacific ; Crawfish ; Croaker, Atlantic; Haddock; Pike; Plaice, European; Pollock; Saith; Sole; Tilapia <b>SHELLFISH:</b> Clams; Cockle; Cuttlefish; Oysters; Periwinkle; Scallops; Scampi; Sea urchin; St James shells; Whelk	<b>FISH:</b> Flatfish; John Dory; Flatfish; Perch, Ocean and Mullet; Sweetfish; Wolf fish <b>SHELLFISH:</b> Mussels; Prawn; Squid	<b>FISH:</b> Redfish; Smelt; Salmon, Pacific (farmed & wild); Salmon, Atlantic (wild) <b>SHELLFISH:</b> Crab, spider; Swincrab	<b>FISH:</b> Anchovy; Herring; Mackerel; Mackerel, Chub; Rainbow trout; Salmon, Atlantic (farmed); Sardines Sprat <b>FISH LIVER:</b> Cod, Atlantic (liver); Saith (liver) <b>SHELLFISH:</b> Crab (brown meat)
	0.1 < x ≤ 0.5 µg/g	<b>FISH:</b> Anglerfish; Catshark; Dab; Grenadier; Grouper; Gurnard; Hake; Ling; Lingcod and Scorpionfish; Nile perch; Pout; Ray; Snapper, Porgy, and Sheephead; Tuna, yellowfin; Tusk; Whiting <b>SHELLFISH:</b> Lobster; Lobsters, American	<b>FISH:</b> Bass, Freshwater; Carp and Buffalo fish; Perch, Freshwater; Scorpion fish; Skate; Tuna; Tuna, Albacore <b>SHELLFISH:</b> Crab; Lobster, Norway; Lobsters, Spiny	<b>FISH:</b> Bass, Saltwater; Bluefish; Goatfish; Halibut, Atlantic; Halibut, Greenland ; Mackerel, Horse; Mackerel, Spanish ; Seabass; Seabream; Tilefish, Atlantic; Tuna, skipjack	<b>FISH:</b> Eel; Mackerel Pacific; Sablefish; Tuna, Pacific bluefin
	0.5 < x ≤ 1.0 µg/g	<b>FISH:</b> Alpacino; Marlin; Orange Roughy; Tuna, bigeye	<b>FISH:</b> Mackerel, King; Shark	<b>FISH:</b> Emperor	
	> 1.0 µg/g		<b>FISH:</b> Swordfish		

## Dioxin-Like Compounds (DLC)

- Fish and EPA+DHA consumption lower the risk of CHD mortality.
- High DLC exposure increases the risk of cancer.
- Established CHD mortality benefits exceed theoretical upper estimate cancer risks for all frequencies and categories of fish consumption and DLC exposure evaluated.



One serving per week

		EPA+DHA			
		< 3 mg/g	3 < 8 mg/g	8 < 15 mg/g	> 15 mg/g
DLC	≤ 1.0 pg/g	+50 -9829	+50 -25870	+50 -50246	+50 -71164
	1.0 ≤ 4.0	+600 -9829	+600 -25870	+600 -50246	+600 -71164
	4.0 ≤ 8.0	+1300 -9829	+1300 25870	+1300 -50246	+1300 -71164
	> 8.0	+4760 -9829	+4760 25870	+4760 -50246	+4760 -71164

\* Assuming DHA ratio 0.67

Two servings per week

		EPA+DHA			
		< 3 mg/g	3 < 8 mg/g	8 < 15 mg/g	> 15 mg/g
DLC	≤ 1.0 pg/g	+100 -19170	+100 -48354	+100 -71164	+100 -71164
	1.0 ≤ 4.0	+1200 -19170	+1200 -48354	+1200 -71164	+1200 -71164
	4.0 ≤ 8.0	+2600 -19170	+2600 -48354	+2600 -71164	+2600 -71164
	> 8.0	+9520 -19170	+9520 -48354	+9520 -71164	+9520 -71164

\* Assuming DHA ratio 0.67

Seven servings per week

		EPA+DHA			
		< 3 mg/g	3 < 8 mg/g	8 < 15 mg/g	> 15 mg/g
DLC	≤ 1.0 pg/g	+350 -59352	+350 -71164	+350 -71164	+350 -71164
	1.0 ≤ 4.0	+4200 -59352	+4200 -71164	+4200 -71164	+4200 -71164
	4.0 ≤ 8.0	+9100 -59352	+9100 -71164	+9100 -71164	+9100 -71164
	> 8.0	+33300 -59352	+33300 -71164	+33300 -71164	+33300 -71164

\* Assuming DHA ratio 0.67

## Factors that might affect risks and benefits of consuming fish and sea mammals

Position in the food chain

Age of animal to be eaten

Fatty acid composition

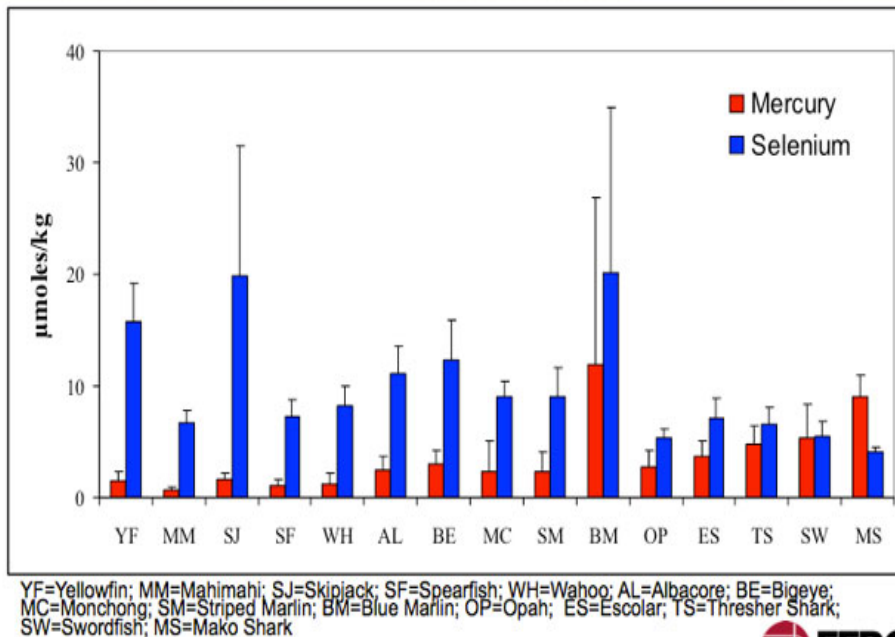
Micronutrient content, e.g. selenium



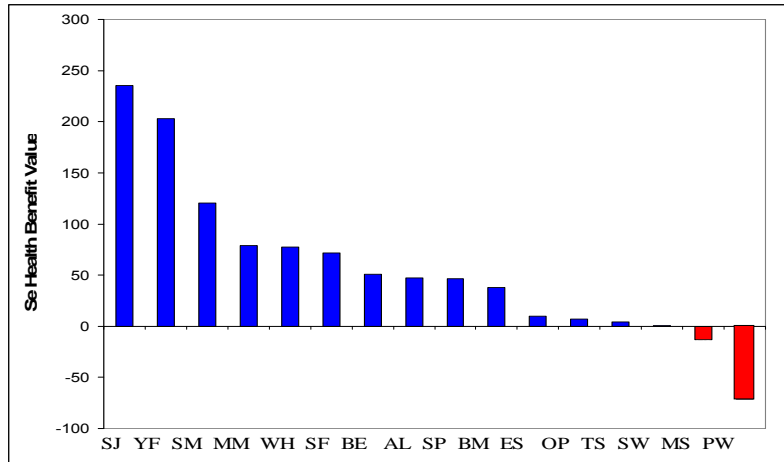
## Selenium in the Mercury Issue

- Methylmercury toxicity does not appear to occur when selenium is present in molar excess of mercury in tissues.
- Methylmercury toxicity occurs because mercury is an irreversible inhibitor of selenoenzymes.
- Biochemical effects of mercury toxicity correspond with expected effects of diminished selenoenzyme activities.

- Selenium-dependent protection against mercury toxicity supports the hypothesis that selenium sequestration is the primary molecular mechanism of mercury toxicity.
- Consumption of selenium-rich ocean fish prevents mercury toxicity rather than contributes to it.
- Consumption of high-mercury, selenium-poor freshwater fish may be far more toxic than is currently expected.




## Selenium Health Benefit Values



YF=Yellowfin; MM=Mahimahi; SJ=Skipjack; SF=Spearfish; WH=Wahoo; AL=Albacore;  
BE=Bigeye; MC=Monchong; SM=Striped Marlin; BM=Blue Marlin; OP=Opah;  
ES=Escolar; TS=Thresher Shark; SW=Swordfish; MS=Mako Shark; PW=Pilot Whale

## Takk for merksemda !






## More to it – benefits from mammals?

*E. Elvevoll*  
 Faculty of Biosciences, Fisheries and Economics (BFE)  
 University of Tromsø, Norway  
 København 14012011

**UNIVERSITETET I TROMSØ UIT**

### Betydning av et marint kosthold for hjertekarsykdom; "Eskimoene - lite hjerte- og karsykdommer"...

*1978 Dyerberg og Bang, Lancet*



#### Omega-6 og Omega-3 forholdet i kroppen og dødsfall forårsaket av hjerte-karsykdommer

	$\Omega$ -6/ $\Omega$ -3	Hjerte-kar dødsfall (% årsak)
Europa, USA	50	45%
Japan	12	12%
Grønlandske eskimoer	1	7%

*(Kromann and Green, ACTA Med Scand 1980; 208: 401)*

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## Eskimo studies

Dietary & blood lipid characteristics of Greenland Eskimos		
Variable	Eskimos	Danes
<i>Dietary intake</i>		
Protein (% energy)	26.0	11.0
Fat (% energy)	37.0	42.0
Carbohydrate (% energy)	37.0	47.0
Saturated fat (% total fat)	22.8	52.7
MUFA (% total fat)	57.3	34.6
PUFA (% total fat)	19.2	12.7
n-6 PUFA (g)	5.4	10.0
n-3 PUFA (g)	13.7	2.8
<i>Blood lipid values</i>		
Total cholesterol (mmol/l)	5.33 ± 0.78	6.24 ± 1.00
Triglycerides (mmol/l)	0.61 ± 0.44	1.32 ± 0.53

Adapted from Kroman & Green, ACTA Med Scand, 1980

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## Seafood consumption is well documented to be beneficial

- Greenland Eskimos, on traditional diet – lower incidence of CHD
- n-3 protects against atherosclerosis and thrombosis
  - raw or minimal processed food
  - visceral organs (liver kidney heart)
  - marine mammals
  - fish

Dyerberg et al., 1978

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### Effect of Marine Oils Supplementation on Coagulation and Cellular Activation in Whole Blood

Bjarne Østerud<sup>a,\*</sup>, Edel Elvevoll<sup>b</sup>, Harald Barstad<sup>b</sup>, Jan Brox<sup>c</sup>, Hanne Halvorsen<sup>a</sup>, Karin Lia<sup>a</sup>, Jan Ole Olsen<sup>a</sup>, Ragnar L. Olsen<sup>a</sup>, Charlotte Sissener<sup>a</sup>, Øystein Rekdal<sup>d</sup>, and Eva Vognild<sup>a</sup>

Departments of <sup>a</sup>Biochemistry and <sup>b</sup>Biootechnology, Institute of Medical Biology, University of Tromsø, <sup>c</sup>Norwegian Institute of Fisheries and Aquaculture Ltd., 9037 Tromsø and <sup>d</sup>Hammerfest Hospital, 9600 Hammerfest, Norway


**ABSTRACT:** A study was performed to explore the effects of supplemental intake of various marine oils known to be part of the Eskimo diet. Healthy men and women (134) were randomly selected to consume 15 mL/d of oil from blubber of seal, cod liver, seal/cod liver, blubber of Minke whale, or no oil for ten weeks. Total cholesterol was unchanged in the oil groups, whereas high density lipoprotein cholesterol increased 7% in the seal/cod liver oil (CLO) group ( $P < 0.05$ ) and 11% in the whale oil group ( $P < 0.005$ ). Triacylglycerol was significantly reduced in the CLO group only. The concentration of prothrombin fragment 1 + 2 was reduced 25% ( $P < 0.05$ ) after whale oil supplementation. No change in fibrinogen or factor VIIc was detected. Tumor necrosis factor generation in lipopolysaccharide (LPS)-stimulated blood was 30% reduced after whale oil ( $P < 0.05$ ), but was unaffected by intake of seal or CLO. The LPS-induced tissue factor activity in monocytes was reduced to a significant degree only in the seal/CLO group (34%) and whale oil group (35%) ( $P < 0.05$ ). The most dramatic change in thromboxane B<sub>2</sub> in LPS-stimulated blood was seen after whale oil intake with 44% reduction ( $P < 0.01$ ). Supplementation of a regular diet with a combination of seal oil and CLO and especially with whale oil seems to have beneficial effects on several products thought to be associated with cardiovascular and thrombotic diseases.

*Lipids* 30, 1111–1118 (1995).

Although several recent studies have shown that a large intake of n-3 fatty acids is beneficial with regard to lowering blood pressure (2), reducing triacylglycerols (3), and modulation of cell function and cell reactivity to external stimuli (4–7), the final conclusion depends on more controlled studies (8). One of the reasons for this is that when epidemiological data relating fish consumption to cardiovascular disease were corrected for covariants, the results were controversial (9,10). The putative role of n-3 fatty acids from fish oil on the development of coronary heart disease has been questioned (11).

Although the low death rate from coronary heart disease among the Eskimos of Greenland has been suggested to stem in large part from their consumption of fish, one should keep in mind that the daily diet of Eskimos living in the traditional way consists of substantial quantities of meat and fat (blubber) from seals and whales (12). The fat composition of seals and especially whales differs significantly from that of fish (13). Hence, one may ask whether oil from these animals may be better candidates than fish oil in explaining the apparent protective effect of the Greenland Eskimo diet. So far no controlled studies pertinent to any effects of these oils have been performed.

In this study we have raised the question as to whether seal and whale oils are more effective than cod liver oil (CLO) in changing biological parameters that might be important in ex-



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### 1990-92; Mimicking the Eskimos - administration of marine oils (15 ml) for 10 weeks

Parameter	Kontrol	Sel	Tran	Sel/Tran	Hval*
<b>Serum:</b> Triacylglycerol (TAG)	basal	-	L*	-	-
Total cholesterol	"	-	-	-	-
HDL cholesterol	"	-	-	H*	H***
<b>Coagulation factors:</b>					
Prothrombin F1 + 2	"	-	-	-	L*
<b>Lipopolysaccharide stimulated(LPS) whole blood:</b>					
Tumornecrosis factor - a activity TNFa (monocytes)	"	-	-	-	L*
Tissue factor activity (TF) (monocytes)	"	-	-	L*	L*
Thromboxane B2 (TXB2)	"	-	-	-	L**

• "Virgin" Kaldpresset hvalolje  
 • no significative, L lower, H higher, \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.005$

*Østerud et al., 1995 Lipids*  
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### THE FATTY ACID COMPOSITION OF THE MARINE OILS

FA (AREAL %)	Cod liver oil	Seal oil	Whale oil
<b>Saturated</b>	<b>15.4</b>	<b>14.3</b>	<b>16.2</b>
<b>Monounsaturated</b>	<b>48.3</b>	<b>49.3</b>	<b>62.3</b>
- 16:1	7.2	10.9	9.5
- 18:1	20.4	21.8	22.1
- 20:1	12.9	11.4	18.5
- 22:1	7.3	5.0	11.8
<b>n - 3</b>	<b>25.9</b>	<b>25.6</b>	<b>12.6</b>
- 20:5 (EPA)	9.8	7.4	3.5
- 20:5 (DPA)	1.1	3.9	2.3
- 22:6 (DHA)	15.0	14.3	6.8

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1990-92;  
Mimicking the Eskimos - administration of marine oils (15 ml) for 10 weeks

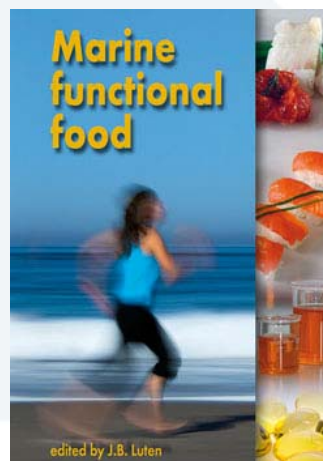
Parameter	Kontrol	Sel	Tran	Sel/Tran	Hvalolje
Serum: Triacylglycerol (TAG)	basal	-	L*	-	-
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HDL cholesterol	"	-	-	H*	H***
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Prothrombin F1 + 2	"	-	-	-	L*
<b>Lipopolysaccharide stimulated(LPS) whole blood:</b>					
Tumornecrosis factor - a activity TNFa (monocytes)	"	-	-	-	L*
Tissue factor activity (TF) (monocytes)	"	-	-	L*	L*
Thromboxane B2 (TXB2)	"	-	-	-	L**

• "Virgin" Kaldpresset hvalolje  
 • no significative, L lower, H higher, \* p< 0.05, \*\* p< 0.01, \*\*\* p< 0.005

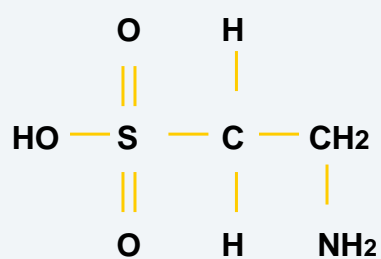
Osterud et al., 1995 Lipids

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- To a large extent attributed to n-3 fatty acids...
- More to it ? OR Other possible contributors
  - Peptides
    - Antioxidative peptides
    - ACE – inhibitors
  - Amino acids
    - Taurine
  - Minerals and trace elements
  - Vitamins
  - .....



## Taurine



Free sulfonated amino acid  
 Marker of seafood consumption



## Health effects - Taurine

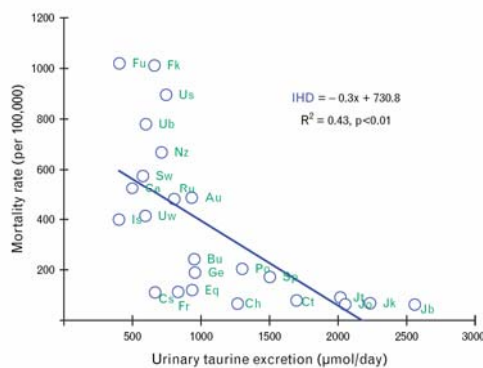
- Higher in seafood
- Involved in many physiological processes
  - Regarded as conditionally essential
  - Added to infant formulas
  - Regarded important in neurological development
- Suggested cardio protective effects
  - Influence cardiovascular risk factors
  - Indirect antioxidative properties – Reduce proinflammatory products
  - Suppress atherosclerosis, platelet aggregation
- **Compared to n-3 PUFA – documentation of health effects is scarce**



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## Dietary markers on IHD mortality

- associations with taurine excretion



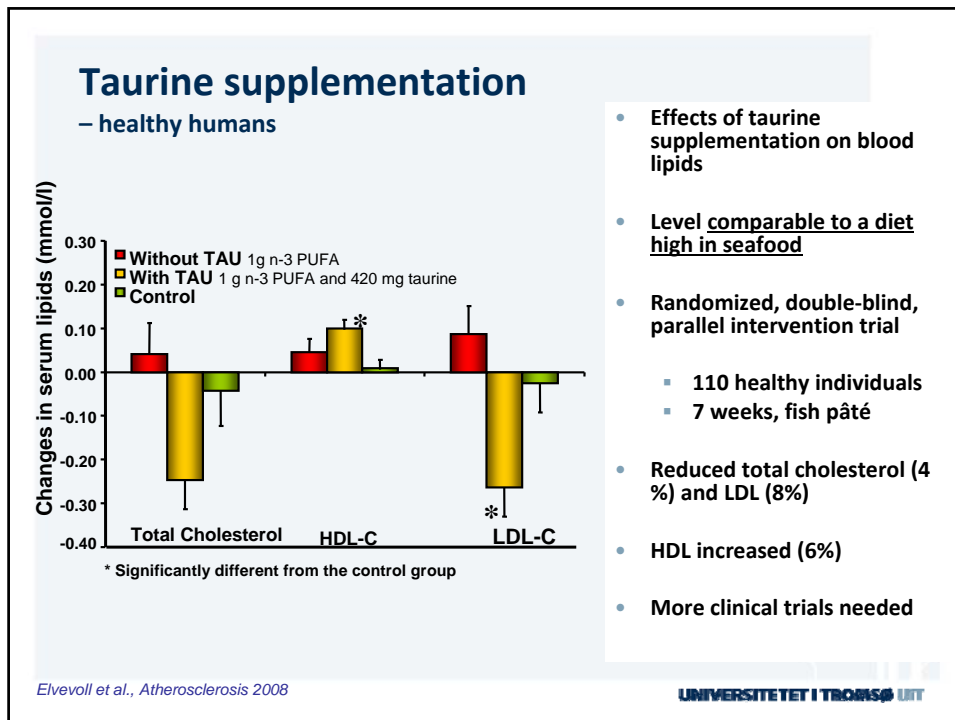
- Associations between various dietary markers and mortality from IHD

- Males, n=2462




- “In our present study, taurine excretion, in fact, appears as the most significant factor (inversely) in IHD mortality”

Yamori et al., J. Hypertension, 2006

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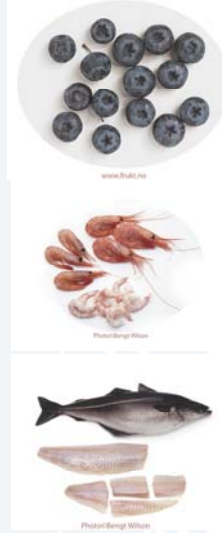
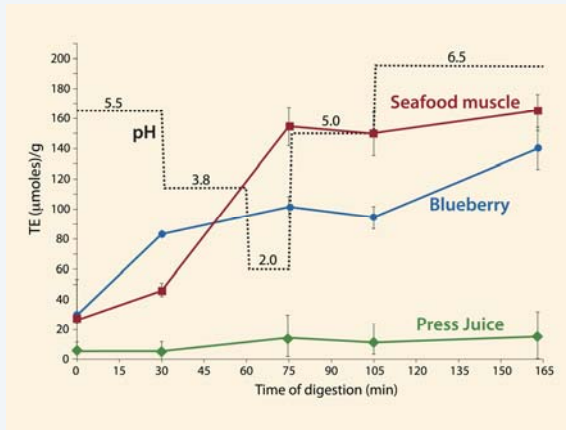
### Getting information on health effects

<h4>Human studies, clinical trials</h4>  <p><b>Highest level of evidence</b></p> <ul style="list-style-type: none"> <li>-Firm control of diet, study length, type of subjects, etc.</li> <li>-Expensive</li> <li>-Impossible to conduct on some diseases</li> </ul>	<h4>Observational (Epidemiological) studies</h4>  <p><b>Segment of population observed</b></p> <ul style="list-style-type: none"> <li>-Fish intake associated with diseases</li> <li>-Indication of correlation</li> <li>-Many confounding factors</li> </ul>
<h4>Animal Studies</h4>  <p><b>Extrapolation to humans is limited</b></p> <ul style="list-style-type: none"> <li>-Can exert tight control over experimental conditions</li> <li>-Insights into designing human studies</li> </ul>	<h4>In vitro (test tube) studies</h4>  <p><b>Hardest to extrapolate to humans</b></p> <ul style="list-style-type: none"> <li>-Important in early phases</li> <li>-Can give directions</li> </ul>

**marfunc** I. Undeland Sept 2008

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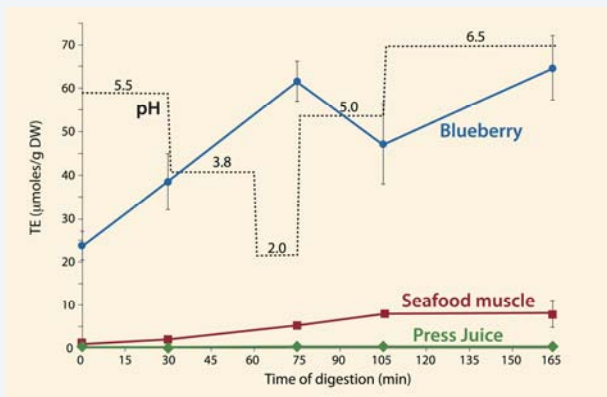
### Antioxidative Capacity (ORAC) of Seafood Items and Blueberry



Antioxidative capacity (ORAC) in samples collected at five time points during *in vitro* digestion of seafood and the corresponding of blueberry. *Jenssen I.J. et.al (2010) J. Agric. Food Chem.*

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### Antioxidative Capacity (FRAP) of Seafood Items and Blueberry



Antioxidative capacity (FRAP) in samples collected at five time points during *in vitro* digestion of seafood muscle and the corresponding of blueberry. *Jenssen I.J. et.al (2010) J. Agric. Food Chem.*

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## Methods (assessing AOC) and results;

- **Oxygen Radical Absorbance Capacity (ORAC)**
  - Preformed peroxy radicals attack a fluorescent probe and decrease the fluorescence. Antioxidants have a protective effect: donate H-atom and delays the decrease in fluorescent.
  - pH 7.4 and 37°C. Trolox as standard.
- **Ferric Reducing Ability of Plasma (FRAP)**
  - Measures the reducing capacity of an antioxidant to reduce a  $Fe^3$ -complex to a  $Fe^{2+}$ -complex with an intense blue colour.
  - pH 3.6 and 37°C. Trolox as standard.
- **AOC**
  - Increase up until the phase simulating the small intestine.
  - Muscle > ten times > related PJs.
  - ORAC: muscle > blueberry
  - FRAP: muscle < blueberry
- **FRAP assay pH 3.6:**
  - Better method to assess protectin in "stomach" environment?
  - appropriate to use when assessing the antioxidative protection in this environment.
- **ORAC assay pH 7.4**
  - better method to assess the antioxidative protection in the intestine and elsewhere in the human body.



Jenssen I.J. et al (2010) *J. Agric. Food Chem.*

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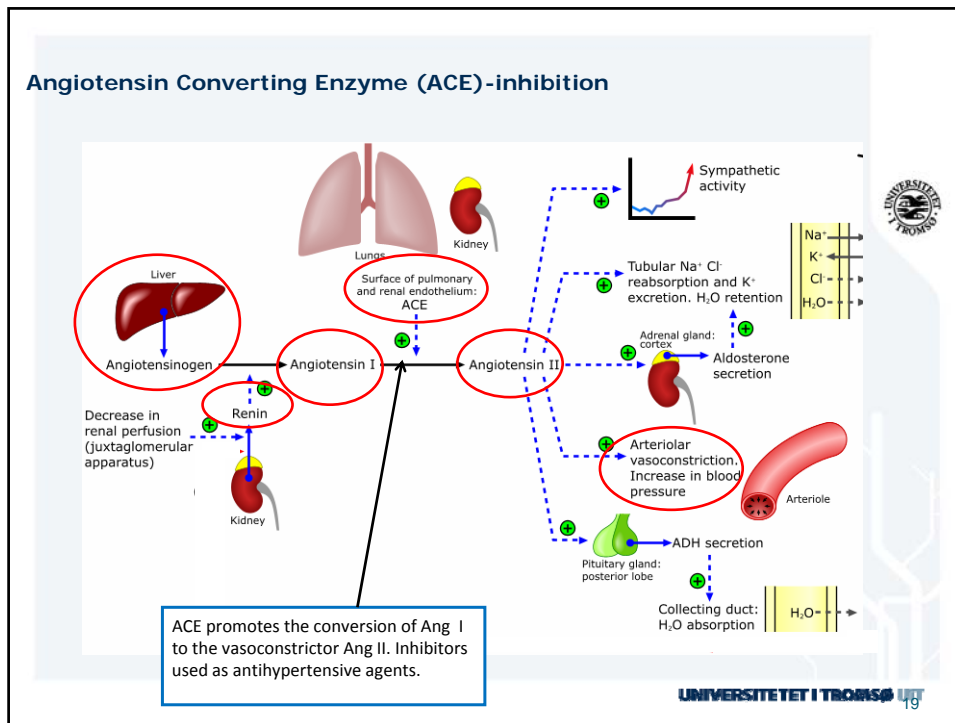
## Antihypertensive (ACE inhibitory) peptides



- Elevated blood pressure is a major independent risk factors for CVD
- Studies in animal models (SHR) and hypertensive human have demonstrated that ACE inhibitory peptides significantly reduce blood pressure.
- The peptides have little or no effect on normotensive subjects.
- The peptides may thus be applied as initial treatment in mildly hypertensive individuals or as supplemental treatment.
- Not associated with side effects reported for synthetic ACE inhibitors such as dry cough, skin rashes and angioedema.



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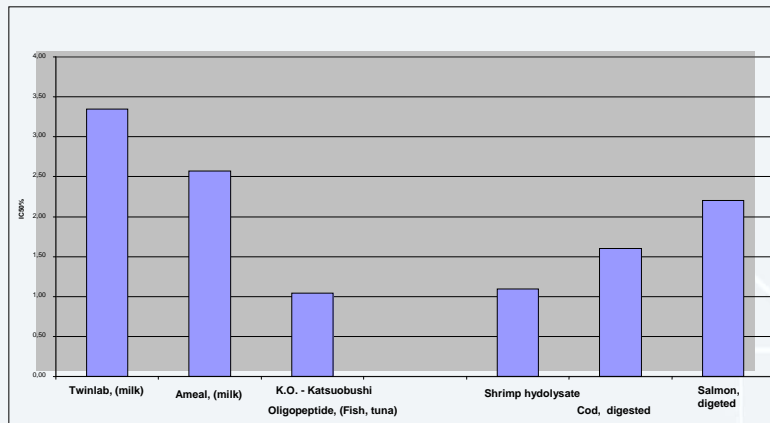
### Marine (and other) ACE inhibiting peptides extensively studied

**Table 1.** ACE inhibitory peptides derived from marine organisms: source, enzyme used for hydrolysis, and IC<sub>50</sub> value.

Source	Enzyme	IC <sub>50</sub>	Ref.
Blue mussel sauce	natural fermentation	19.34 µg/mL	[19]
Alaska pollack	pronase, flavourzyme	0.21 mg/mL	[33]
Alaska pollack	alcalase, pronase, collagenase	2.6 µM	[34]
Big eye tuna (muscle)	pepsin	21.6 µM	[35]
Big eye tuna (frame)	pepsin	11.28 µM	[36]
Shrimp	protease	0.39 µM	[37]
Shrimp	<i>Lactobacillus fermentum</i> enzymes	3.37 mg/mL	[38]
Hard clam	protamex	51 µM	[39]
Sea cucumber	bromelain, alcalase, protease	4.5 µM	[40]
Rotifer	alcalase	9.64 µM	[41]
Wakame	pepsin	21 µM	[42]
Microalga	pepsin	29.6 µM	[43]
Yellow fin sole	α-chymotrypsin	22.3 µM	[44]
Bonito	thermolysin	0.32 µM	[45]
Sardine	alkaline protease	0.015 mg/mL	[46]
Oyster	pepsin	66 µM	[47]
Shark	protease	1.45 µM	[48]
Anchovy fish sauce	natural fermentation	22 µM	[49]
Sea bream	alkaline protease	0.57 mg/mL	[50]

DOCMAR a project initiated by RUBIN to document the effects of marine health promoting ingredients

***In vitro* IC<sub>50</sub> analysis** (µg/mU ACE)



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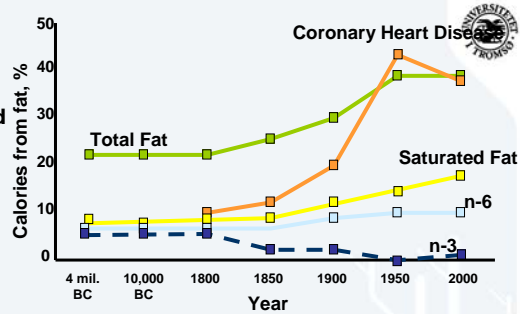
**Mechanisms of cardioprotective effect**

- Lower TAG concentrations in serum
  - Lower blood pressure – Alters blood rheology
  - Heart rate
- Alteration in membrane lipid composition – positive effects on Na, K, Ca channels
  - Anti-arrhythmic
- Less inflammatory
  - Improved endothelial function
  - Reduce atherosclerosis – reduced adhesion
  - Alters composition of plaque – less prone to rupture and thus anti-thrombotic
- A single or combination of effects may explain association between seafood consumption and cardiovascular protection

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## Historical background

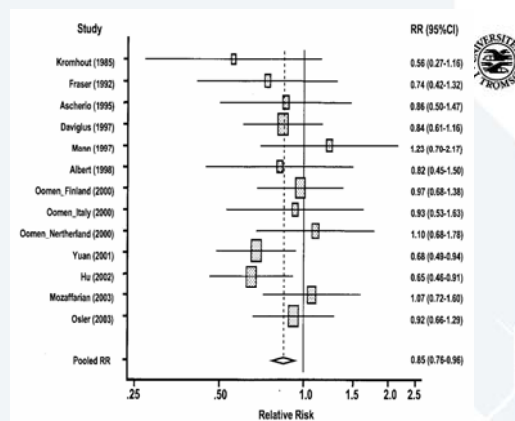
- Old food lore of seafood
  - It makes you smart
  - It makes you stay healthy
- Dietary habits have changed
  - Last 200 years
  - Relative total fat, saturated fat and n-6 increased
  - Relative n-3 decreased
  - Incidents of CHD increased



Adapted from Leaf et al., Am J Clin Nutr, 1987

## Fish consumption and CHD mortality

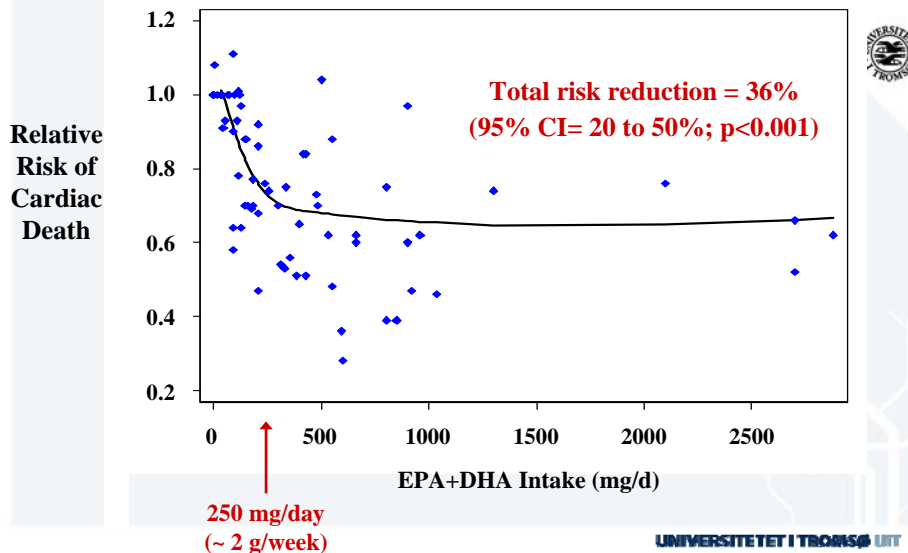
- Meta-analysis, observational, 222.364 individuals
- Inverse association between fish consumption and CHD mortality rates
- Fish meal once a week, reduced risk of CHD death by 15 %
- May be further reduced with additional consumption
  - 7% decrease with per additional serving per week



He et al., Circulation, 2004

Meta-analysis of 16 prospective cohort studies (n=326,572) and 4 randomized controlled trials (n=29,456) from the U.S., Europe, and Asia.

Mozaffarian & Rimm. JAMA 2006



Thank you for listening!



K.E. Eilertsen

J. Brox

I.J. Jensen

R. Larsen

H. Mæhre

B. Østerud

Norwegian Research Council, EU –  
"SeafoodPlus", Danish RC –  
"PEPFISH".

Foto: Ole Torrissen, HI

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*Sjurdur F. Olsen*

Centre for Fetal Programming

Maternal Nutrition Group  
Statens Serum Institut, Copenhagen

Department of Nutrition,  
Harvard School of Public Health,  
Boston

[sfo@ssi.dk](mailto:sfo@ssi.dk)

## Centre for Fetal Programming

- Based on a 5-year grant 2010 to 2015 from the Danish Council for Strategic Research
- Multidisciplinary consortium located at several different institutions
- Main location at Statens Serum Institut, Copenhagen
- Three main pillars
  - Epidemiological pillar
  - Animal experimental pillar
  - Human clinical pillar

## Center Mission and Vision

### *Mission of Center*

- Overall aim ... to **examine** and **understand mechanisms underlying** fetal programming of diseases and development ...



## Maternal Nutrition Group

Mission: To study impact of the diet consumed during pregnancy on health, in the short as well as the long term

Approach: Multi-disciplinary teamwork on epidemiological data

Available research resources:

- Observational studies with comprehensive assessments of dietary intake in pregnancy, and
- Randomised interventions with food supplements to pregnant women

## Cohorts with info on maternal dietary exposures

**The 1988-1989 Aarhus-Observational cohort (n=965)**

**The 1990 Aarhus-Trial cohort (n=533)**

**The 1990-1996 Europe-Trial cohort (FOTIP) (n=1619)**

**The 1994-1997 ABCohort-Observational cohort (n=8700)**

**The 1996-2002 DNBC-Observational cohort (n=92,000)**

**Trial in China (target number: >5,000)**

## Kost til gravide Det videnskabelige grundlag for råd om kost i forbindelse med graviditet



En rapport fra Ernæringsrådet  
af:

Sjúrður F. Olsen  
Lars O. Dragsted  
Harald S. Hansen  
Kim Fleischer Michaelsen  
Nils Milman  
Lars Ovesen  
Tove Petersen  
Ann Tabor

The screenshot shows the website for Nordic Nutrition Recommendations (NNR 5). The page is titled 'Pregnancy and lactation' and lists several experts. The 'Experts' section includes:

- Chair:** Inga Thorsdottir (Professor)  
Unit for Nutrition Research  
Faculty of Food Science and Nutrition  
School of Health Sciences  
University of Iceland & University Hospital  
Eiríksgrata 29  
101 Reykjavík  
Iceland
- Anne Lise Brantsaeter (PhD)**  
Division of Environmental Medicine  
Department of Food Safety and Nutrition  
Norwegian Institute of Public Health  
PO Box 4404 Nydalen  
04030 Oslo  
Norway
- Elisabet Forsum (Professor)**  
Institutionen för klinisk och experimentell medicin  
Linköpings universitet  
581 83 LINKÖPING  
Sweden
- Sjurdur F Olsen (Professor)**  
Maternal Nutrition Group  
Statens Serum Institut  
Artillerivej 5  
2300 Copenhagen S  
Denmark
- Anna Sigrídur Ólafsdóttir (PhD)**  
Human nutrition  
University of Iceland  
School of Education  
Stakkahlíð  
105 Reykjavík

## Impact of marine n-3 fatty acid intake in pregnancy on

- risk of preterm birth,
- risk of asthma and allergies, and
- on cognitive development in the offspring

## Preterm delivery

## Preterm delivery

Does a low intake of long chain n-3 fatty acids increase the risk of preterm delivery?

Does fish oil supplementation prevent preterm delivery?

## Preterm delivery: An important public health issue

Definition: Delivery before 37th week of gestation

Occurs in 5-10% of all pregnancies

A leading cause of perinatal mortality and morbidity in both developed and developing countries

Underlying cause in 85% of deaths of normally formed infants

Survival has improved

*However:*

Costs of intensive care of very premature infants: US\$ 1500 / d

Survivors often suffer from permanent physical and neurological handicap

## The Faeroe Islands

The highest mean birth weight among 33 geographically defined populations from all over the world

### *Birth weight means*

<b>Faeroe Islands</b>	<b>3610 g</b>
<b>Iceland</b>	<b>3560 g</b>
<b>Norway</b>	<b>3500 g</b>
<b>Sweden</b>	<b>3470 g</b>
<b>New Zealand</b>	<b>3420 g</b>
<b>Denmark</b>	<b>3380 g</b>
<b>San Marino</b>	<b>3380 g</b>
<b>England</b>	<b>3350 g</b>

(Olsen & Joensen, J Epidemiol Comm Health 1985)

## The Faeroe Islands

The highest mean birth weight among 33 geographically defined populations from all over the world

### *Birth weight means*

<b>Faeroe Islands</b>	<b>3610 g</b>
Iceland	3560 g
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New Zealand	3420 g
Denmark	3380 g
San Marino	3380 g
England	3350 g

(Olsen & Joensen, J Epidemiol Comm Health 1985)

## The Faeroe Islands

v.

## Denmark

Longer gestations, by approx. 4 days

Higher birth weights, by approx. 200 grams

Half (approx. 100 grams) of the birth weight difference explainable by longer gestations

Higher foetal growth rate

(Olsen et al. Lancet 1986)

## The Faeroe Islands

(Olsen et al. Lancet 1986)

TABLE I—LIVEBORN SINGLETON INFANTS, PRIMIPAROUS MOTHERS

	Faroës 1982–84	Denmark 1983
Number of deliveries	762	22 797
Mean $\pm$ SD*		
Birthweight (g)	3554 $\pm$ 527	3360 $\pm$ 544
Birth length (cm)	52.80 $\pm$ 2.43	51.32 $\pm$ 2.57
Gestation (completed weeks)	40.21 $\pm$ 1.75	39.68 $\pm$ 1.83
Induced deliveries	12.8%	9.4%
Caesarean sections		
Elective	3.7%	3.4%
Emergency	11.3%	10.5%

\*Numbers of unknowns represent less than 2%.

TABLE II—BIRTHWEIGHT STRATIFIED WITH RESPECT TO GESTATION

Completed weeks of gestation	Mean $\pm$ SD birthweight in g (n)		Mean $\pm$ SE difference
	Faroës 1982–84	Denmark 1983	
$\leq$ 37	2629 $\pm$ 694 (34)	2507 $\pm$ 644 (1910)	122 $\pm$ 120
38	3311 $\pm$ 491 (36)	3099 $\pm$ 425 (1931)	212 $\pm$ 82
39	3397 $\pm$ 494 (70)	3292 $\pm$ 423 (3547)	105 $\pm$ 60
40	3555 $\pm$ 464 (284)	3448 $\pm$ 430 (8901)	107 $\pm$ 28
41	3672 $\pm$ 450 (190)	3574 $\pm$ 439 (4164)	98 $\pm$ 33
42	3758 $\pm$ 439 (122)	3669 $\pm$ 455 (2021)	89 $\pm$ 41
$\geq$ 43	3844 $\pm$ 546 (16)	3682 $\pm$ 470 (265)	162 $\pm$ 144
Total	3554 $\pm$ 527 (752)	3360 $\pm$ 544 (22 797)	194 $\pm$ 20

Lancet 1986; 1986: 367-369

Olsen, Hansen, Sørensen et al.

Hypothesis: Intake of marine fat, rich in (n-3)-polyunsaturated fatty acids, may increase birth weight by prolonging gestation

Suggested mechanism: Impact on prostaglandins involved in the parturition process: PGF, PGE, PGI

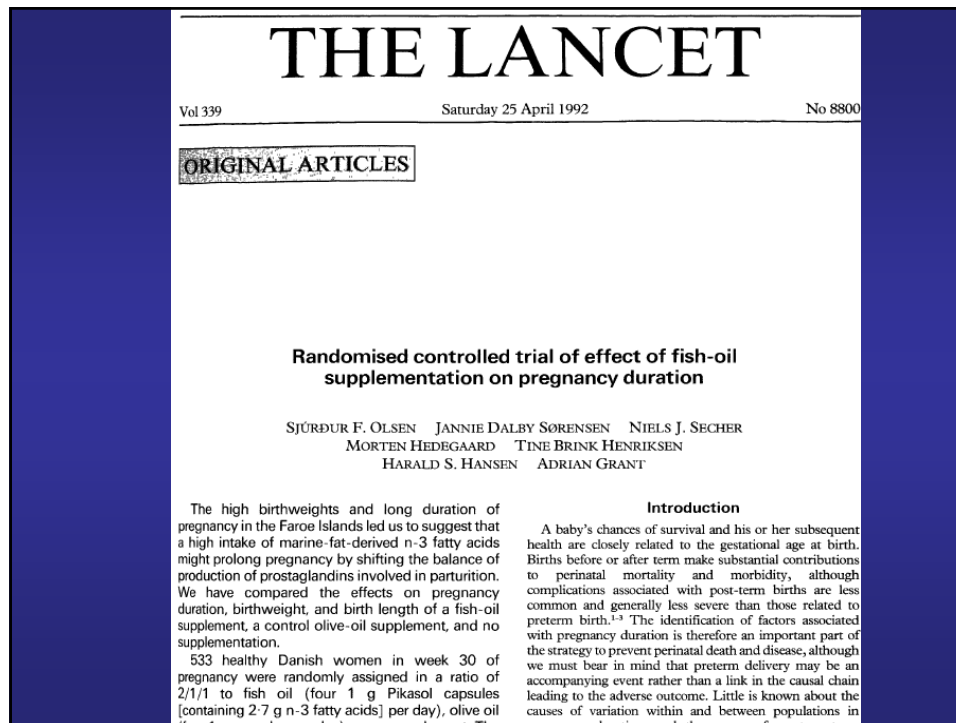
### Marine n-3 fatty acids and preterm delivery – some articles by me and my colleagues

- *Olsen & Joensen. JECH 1985*
  - High birth weights in the Faroes
- *Olsen, Hansen, Sørensen et al. Lancet 1986*
  - Due to marine n-3 fatty acids?
- *Olsen & Hansen. Agents and Actions 1987*
  - A suggestive case story
- *Olsen, Hansen, Jensen. Prostaglandins 1991*
  - Rats receiving fish oil longer gestation
- *Olsen, Olsen, Frische. IJE 1991*
  - Danish women with high fish intake increased foetal growth
- *Olsen, Secher, Sørensen et al. Lancet 1992*
  - Women receiving fish oil longer gestation and higher birth weight
- *Olsen, Grandjean, Weihe, Viderø. JECH 1994*
  - Faroese women with high fish intake increased foetal growth
- *Olsen, Secher, Tabor et al. BJOG 2000*
  - Women receiving fish oil reduced recurrence risk of preterm birth
- *Olsen & Secher. BMJ 2002*
  - Women with low fish consumption increased risk of preterm birth
- *Knudsen VK, Hansen HS, Østerdal ML, Mu H, Mikkelsen TB, Olsen SF. BJOG 2006*
  - No effect detected of supplementation
- *Olsen, Østerdal ML, Salvig JD et al. Eur J Epidemiol 2006*
  - Zero fish intake is a very strong risk factor for preterm birth
- *Olsen, Østerdal ML, Salvig JD et al. E J Clin Nutr 2007*
  - Effect of fish oil supplementation dependent on baseline intake of fish

Lancet 1992; 339; 1003-1007

*Olsen, Sørensen, Secher et al.*

Randomised controlled trial of effect of  
fish oil supplementation on  
pregnancy duration



## Randomised controlled trial in Århus

### *Difference in mean gestation length*

	Fish oil minus olive oil	
	Mean (95% CI)	t-test
All	4.0 (2.2, 12.6) days	p<0.005
<i>Stratified according to fish intake at baseline</i>		
Low	7.4 (2.2, 12.6) days	p<0.01
Middle	4.8 (1.8, 7.8) days	p<0.005
High	-1.6 (-8.4, 5.1) days	p>0.2

(Olsen et al. Lancet 1992)

## Randomised controlled trial in Århus

### *Conclusions*

**Fish oil was associated with delayed delivery**

**Effect seemed to depend on fish intake at baseline**

**No effect detected on foetal growth**

(Olsen et al. Lancet 1992)

British Journal of  
Obstetrics and Gynaecology  
2000; 107: 382-395

*Olsen, Secher, Tabor, Weber, Walker,  
Gluud et al.*

Randomised clinical trials of fish oil  
supplementation in high risk  
pregnancies

## Fish Oil Trial In Pregnancy (FOTIP)

*19 delivery wards in 7 European countries*

*Clinical Centers* (number of women enrolled at each center given in brackets): BELGIUM: Erasmushospital, Borgerhout (21), B.v. Bulck. DENMARK: Aarhus University Hospital, Aarhus (FOTIP Coordinating Centre) (424), N.J. Secher, J.D. Salvig, M. Hedegaard, T.B. Henriksen; Hvidovre Hospital, Copenhagen (350), T. Weber, L.K. Møller; Odense University Hospital, Odense (224), L. Elving, L. Hvidman, L.K. Jensen, B. Ljungström; Rigshospitalet, Copenhagen (218), A. Tabor, H. Nyholm, A.-C. Halvorsen; Glostrup Amtssygehus, Copenhagen (21), J.K. Thomsen, A. Lange; Randers Hospital, Randers (15), I. Qvist. HOLLAND: Free University Hospital, Amsterdam (37), P. Hummel, G. Dekker, F. Althuisius. ITALY: Istituto Di Clinica, Bologna (40), O. Sanlorenzo, C. Orlandi. NORWAY: Haukeland Sykehus, Bergen (24), J. Trovik. RUSSIA: Russian Research Centre for Perinatology, Moscow (21), E.M. Vikhlyaeva, V.A. Bourlev, S.V. Pavlovitch. SWEDEN: Danderyd Sjukhus, Stockholm (61), A. Björklund, M. Nyholm. UNITED KINGDOM: Rutherglen Maternity Hospital, Glasgow (116), S. Björnsson, K. Sullia; Royal Maternity Hospital, Glasgow (46), I.A. Greer; Queen Mother's Hospital, Glasgow (27), T. Johnston, A. Cameron; Sct. James University Hospital, Leeds (20), J.J. Walker, I. Currie; Newham General Hospital, London (15), E.P. Roberts; The Jessop Hospital, Sheffield (12), F. Fairlie, N. Davies.

*Organised from*

Perinatal Epidemiological Research Unit, Skejby University Hospital, Denmark

## Fish Oil Trial In Pregnancy (FOTIP)

### *Prophylactic trials*

**232 women with earlier preterm delivery**

**280 women with earlier intrauterine growth retardation**

**386 women with earlier preeclampsia**

**579 women pregnant with twins**

### *Therapeutic trials*

**79 women threatening preeclampsia**

**63 women with suspected intra uterine growth retardation**

(Olsen, Secher, Tabor et al. Br J Obstet Gynaecol 2000)

## Fish Oil Trials In Pregnancy (FOTIP)

*Intervention products*

Capsules with fish oil v. capsules with olive oil

*Prophylactic trials*

2.7 grams long chain n-3 fatty acids per day

From around gestation week 20 until delivery

*Therapeutic trials*

6.1 grams long chain n-3 fatty acids per day

From around gestation week 33 until delivery

(Olsen, Secher, Tabor et al. Br J Obstet Gynaecol 2000)

## Fish Oil Trials In Pregnancy (FOTIP)

Women having had preterm delivery in an earlier pregnancy

	<i>Fish oil</i>	<i>Olive oil</i>	
	n=108	n=120	
			<i>Odds Ratio (95% CI)</i>
Preterm (n)	21%(23)	33% (40)	0.54 (0.03, 0.98) p=0.05
Early preterm (n)	4.6%(5)	13.3 (16)	0.32 (0.11, 0.89) p=0.04
			<i>Difference (95% CI)</i>
Gestation	269.2 d	260.7 d	8.5 (1.9, 15.2) p=0.01
Birth weight	3169 g	2960 g	209 (27, 390) p=0.02

(Olsen, Secher, Tabor et al. Br J Obstet Gynaecol 2000)

## Fish Oil Trials In Pregnancy (FOTIP)

*Combined trials (n = 1619)*

Fish oil group had delayed timing of spontaneous delivery compared to olive oil group

Proportional hazards ratio: 1.22 (95% CI 1.07, 1.39, p=0.002)

Elective deliveries regarded as censoring event

(Olsen, Secher, Tabor et al. Br J Obstet Gynaecol 2000)



## Observational study: Prospective cohort in Århus, Denmark

*Association between fish intake and risk of preterm delivery:*

*Total N = 8729*

*Selected exposure groups*

Fish as warm&cold food	n	Preterm	Odds Ratio	
			Crude	Adjusted*
Never	282	7.1%	3.79	3.60
<1 per month	301	4.7%	2.34	2.09
1-3 per month	511	3.5%	1.59	1.58
1+ per week	210	1.9%	1.00	1.00

*\*) Adjusted for smoking, alcohol, age, parity, height, pre-pregnant weight, educational status, cohabitant status*

*(Olsen & Secher, BMJ 2002)*

## Marine n-3 fatty acids and preterm delivery: recent reviews

*Makrides M, Duley L, Olsen SF. Marine oil, and other prostaglandin precursor, supplementation for pregnancy uncomplicated by pre-eclampsia or intrauterine growth restriction. Cochrane Database Syst Rev. 2006 Jul 19;3:CD003402*

*Jensen CK. Effects of n-3 fatty acids during pregnancy and lactation. Am J Clin Nutr 2006 Jun;83(6 Suppl):1452S-1457S.*

*Szajewska H, Horvath A, Koletzko B. Effect of n-3 long-chain polyunsaturated fatty acid supplementation of women with low-risk pregnancies on pregnancy outcomes and growth measures at birth: a meta-analysis of randomized controlled trials. Am J Clin Nutr 2006 Jun;83(6):1337-44*

*Horvath A, Koletzko B, Szajewska H. Effect of supplementation of women in high-risk pregnancies with long-chain polyunsaturated fatty acids on pregnancy outcomes and growth measures at birth: a meta-analysis of randomized controlled trials. Br J Nutr. 2007 Apr 10;:1-7*

**All 4 reviews conclude: "Marine n-3 fatty acids prolong pregnancy, but this effect may not be clinically important"**

## A recently published study

ORIGINAL CONTRIBUTION

JAMA. 2010;304(15):1675-1683 (doi:10.1001/jama.2010.1507)

**JAMA**<sup>®</sup>

### Effect of DHA Supplementation During Pregnancy on Maternal Depression and Neurodevelopment of Young Children

A Randomized Controlled Trial

Maria Makrides, BSc, BND, PhD  
 Robert A. Gibson, BSc, PhD  
 Andrew J. McPhee, MBBS  
 Lisa Yelland, BSc  
 Julie Quinlivan, MBBS, PhD  
 Philip Ryan, MBBS, BSc  
 and the DOMInO Investigative Team

**Context** Uncertainty about the benefits of dietary docosahexaenoic acid (DHA) for pregnant women and their children exists, despite international recommendations that pregnant women increase their DHA intakes.

**Objective** To determine whether increasing DHA during the last half of pregnancy will result in fewer women with high levels of depressive symptoms and enhance the neurodevelopmental outcome of their children.

**Design, Setting, and Participants** A double-blind, multicenter, randomized controlled trial (DHA to Optimize Mother Infant Outcome [DOMInO] trial) in 5 Australian maternity hospitals of 2399 women who were less than 21 weeks' gestation with singleton pregnancies and who were recruited between October 31, 2005, and January 11, 2008. Follow-up of children (n=726) was completed December 16, 2009.

**Intervention** Docosahexaenoic acid-rich fish oil capsules (providing 800 mg/d of DHA) or matched vegetable oil capsules without DHA from study entry to birth.

**E**PIDEMIOLOGICAL INVESTIGATIONS from the United States and Europe demonstrate that higher intakes of n-3 long-chain poly-

## DHA SUPPLEMENTATION DURING PREGNANCY AND MATERNAL DEPRESSION

**Table 4.** Secondary Clinical Outcomes<sup>a</sup>

Outcomes	DHA Supplement (n = 1197)	Control Supplement (n = 1202)	Unadjusted		Adjusted <sup>b</sup>	
			Effect (95% CI)	P Value	Effect (95% CI)	P Value
Duration of gestation, median (IQR), d	282 (275-288)	281 (275-287)	NA	.05 <sup>c</sup>	NA	.05 <sup>c</sup>
Birth <37 wk gestation	67 (5.60)	88 (7.34)	0.76 (0.56 to 1.04)	.09	0.77 (0.56 to 1.05)	.09
Birth <34 wk gestation	13 (1.09)	27 (2.25)	0.49 (0.25 to 0.94)	.03	0.49 (0.25 to 0.94)	.03
Postterm induction or postterm prelabor cesarean delivery	211 (17.59)	165 (13.72)	1.28 (1.06 to 1.55)	.01	1.28 (1.06 to 1.54)	.01
Birth by cesarean delivery	326 (27.25)	350 (29.14)	0.94 (0.82 to 1.06)	.31	0.94 (0.83 to 1.07)	.34
Log blood loss at birth, mean (SD)	5.64 (0.59)	5.65 (0.60)	-0.01 (-0.06 to 0.04)	.79	-0.01 (-0.05 to 0.04)	.79
Postpartum hemorrhage	57 (4.72)	64 (5.28)	0.89 (0.62 to 1.28)	.54	0.90 (0.63 to 1.28)	.55
Birth weight, mean (SD), g	3475 (564)	3407 (576)	69 (23 to 115)	.003	68 (23 to 114)	.003
Birth weight z score, mean (SD)	0.28 (1.06)	0.22 (1.02)	0.06 (-0.02 to 0.15)	.16	0.06 (-0.02 to 0.14)	.16
Birth weight <2500 g	41 (3.41)	63 (5.27)	0.65 (0.44 to 0.95)	.03	0.65 (0.44 to 0.96)	.03

Abbreviations: CI, confidence interval; DHA, docosahexaenoic acid; IQR, interquartile range; NA, not applicable.

<sup>a</sup>Data are expressed as No. (%) with effect being relative risk or mean (SD) with effect being difference in means, unless otherwise indicated. All values are based on analysis of 50 imputed datasets.

<sup>b</sup>Adjusted for confounding and parity (birth <34 weeks' gestation adjusted for parity only).

<sup>c</sup>Based on a stratified log-rank test.

Maria Makrides; Robert A. Gibson; Andrew J. McPhee; et al.  
JAMA. 2010;304(15):1675-1683

Ongoing study

## Trial in low fish intake areas in China

Sites: Cities of **Lan Zhou** (Gansu) and **Xi'an** and **Wei Nan** (Xiaanxi)

Study Director: **SF OLSEN**, Center for Fetal Programming, Denmark  
PI: **ZHOU W**, Shanghai Inst Planned Parenthood Res, China

Recruitment during 2008-2011

Goal number: > **5,000** pregnant women (**9,000**)

Intervention regimens: capsules from **gestation weeks 20 to 37** providing

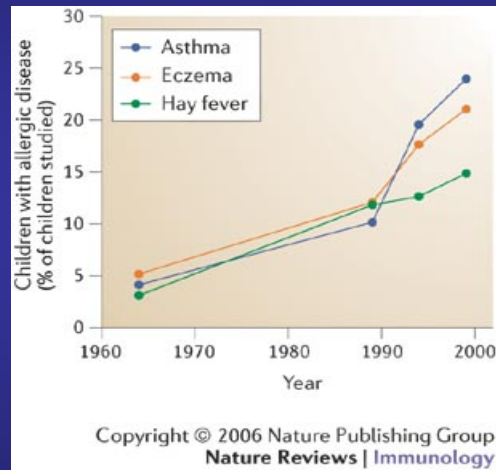
- **0.5 grams** per day marine n-3PUFA
- **2.0 grams** per day marine n-3PUFA
- **0 grams** per day marine n-3PUFA

Two general dietary assessments: at baseline and at gestation week 30  
(**Obervational component**)

Main endpoints: **preterm birth**, GDM, child atopy, child cognitive development

## Asthma and allergy

## Time Trends in Allergic Disease



Devereux G, *Nature Reviews Immunol.*, 2006.

## Maternal diet and atopic diseases in child

- The case for in-utero origin of atopic diseases
  - Most atopic cases appear in early childhood
  - Perinatal factors (birth weight, preterm birth, maternal smoking etc.) are associated with asthma risk
  - The ratio between Th1/Th2-cells in the immune system play an important role in asthma, and the critical period of establishment of the Th1/Th2 balance is in the early life period

## Asthma and allergy

*Possible nutritional explanations for the rise in asthma prevalence:*

- Increase in intake of linoleic acid
- Reduction in intake of marine n-3 fatty acids
- Reduction in intake of vitamin D

## Asthma and allergy

*At the moment there is limited empirical evidence for involvement of maternal exposures to linoleic acid or vitamin D*

*A few studies support that marine n-3 fatty acids play a role*

*> only 1RCT yet with long-term follow-up*

## Marine N-3PUFA and asthma and allergy

### Case-control studies

- *Calvani M, Alessandri C, Sopo SM et al. Consumption of fish, butter and margarine during pregnancy and development of allergic sensitizations in the offspring: role of maternal atopy. *Pediatr Allergy Immunol* 2006;17:94.*
- *Salam MT, Li YF, Langholz B, Gilliland FD. Maternal fish consumption during pregnancy and risk of early childhood asthma. *J Asthma* 2005;42:513.*

### Cohorts, findings compatible with preventive effect of marine n-3PUFA

- *Willers S, Devereux G, Craig L et al. Maternal food consumption during pregnancy and asthma, respiratory and atopic symptoms in 5-year-old children. *Thorax* 2007.*
- *Romieu I, Torrent M, Garcia-Esteban R et al. Maternal fish intake during pregnancy and atopy and asthma in infancy. *Clin Exp Allergy* 2007;37:518.*
- *Sausenthaler S, Koletzko S, Schaaf B et al. Maternal diet during pregnancy in relation to eczema and allergic sensitization in the offspring at 2 y of age. *Am J Clin Nutr* 2007;85:530.*

### Cohorts, 'negative'

- *Newson RB, Shaheen SO, Henderson AJ, Emmett PM, Sherriff A, Calder PC. Umbilical cord and maternal blood red cell fatty acids and early childhood wheezing and eczema. *J Allergy Clin Immunol* 2004;114:531*

## Marine N-3PUFA and asthma and allergy

### RCTs

*Denburg JA, Hatfield HM, Cyr MM et al. Fish oil supplementation in pregnancy modifies neonatal progenitors at birth in infants at risk of atopy. *Pediatr Res* 2005;57:276-81.*

*Dunstan JA, Mori TA, Barden A et al. Fish oil supplementation in pregnancy modifies neonatal allergen-specific immune responses and clinical outcomes in infants at high risk of atopy: a randomized, controlled trial. *J Allergy Clin Immunol* 2003;112:1178-84.*

*Barden AE, Mori TA, Dunstan JA et al. Fish oil supplementation in pregnancy lowers F2-isoprostanes in neonates at high risk of atopy. *Free Radic Res* 2004;38:233-9.*

*Prescott SL, Barden AE, Mori TA, Dunstan JA. Maternal fish oil supplementation in pregnancy modifies neonatal leukotriene production by cord-blood-derived neutrophils. *Clin Sci (Lond)* 2007;113:409-16.*

## Marine N-3PUFA and asthma and allergy

RCTs – mainly biochemical end points (n < 200)

Denburg JA, Hatfield HM, Cyr MM et al. Fish oil supplementation in pregnancy modifies neonatal progenitors at birth in infants at risk of atopy. *Pediatr Res* 2005;57:276-81.

Dunstan JA, Mori TA, Barden A et al. Fish oil supplementation in pregnancy modifies neonatal allergen-specific immune responses and clinical outcomes in infants at high risk of atopy: a randomized, controlled trial. *J Allergy Clin Immunol* 2003;112:1178-84.

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Prescott SL, Barden AE, Mori TA, Dunstan JA. Maternal fish oil supplementation in pregnancy modifies neonatal leukotriene production by cord-blood-derived neutrophils. *Clin Sci (Lond)* 2007;113:409-16.

## Randomised controlled trial in Århus

### Design

533 healthy women in 30<sup>th</sup> week of gestation

Randomised to fish oil, olive oil or no oil

Oils were provided in identical looking capsules

(Olsen et al. *Lancet* 1992)

Children born 1990 - registry linkage study

## Fish oil RCT in Århus 1990

### Conclusions so far from the trial

Fish oil was associated with longer pregnancy

*(Lancet 1992)*

Fish oil impacted maternal thromboxane and prostacyclin production

*(Am J Obstet Gynecol 1994)*

Fish oil raised concentrations of n-3 fatty acids in umbilical cord blood and vessels walls

*(Br J Nutr 1995)*

## Fish oil RCT in Århus 1990

From the 533 singleton pregnancies randomised in 1990, we identified 528 children alive and still living in Denmark in 2006, according to the national central personal registry

Registry extractions were made from the mandatory National Patient Registry:

all asthma related diagnoses given in relation to any hospital encounter were identified

## Fish oil RCT in Århus 1990

### 16 year registry based follow up

For each child we extracted information regarding the following diagnoses given during the period from birth of the child in 1990 until August 2006:

ICD10 codes DJ45 (asthma)

DJ450 (allergic asthma)

DJ451 (asthma bronchiale non allergicum)

DJ458 (asthma of mixed type)

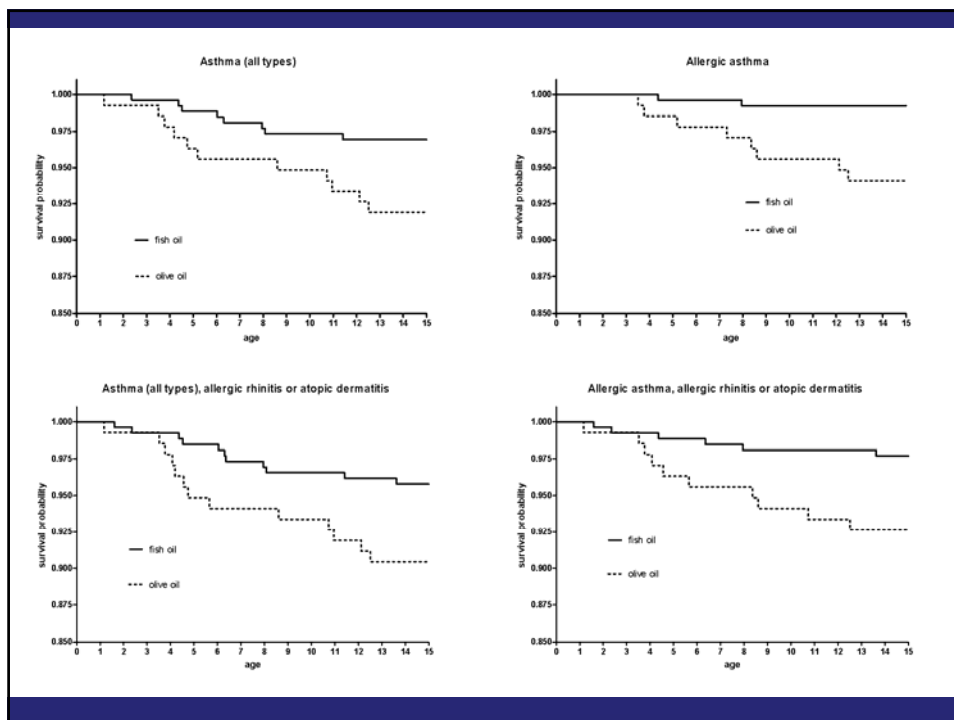
DJ459 (asthma without specification)

DJ469 (status asthmaticus)

DJ 301-304 (allergic rhinitis)

DL200, DL208, DL208A, DL209 (atopic dermatitis)

Corresponding ICD8 codes 49300, 49301, 49302, 49308, 49309 and 69100



Olsen SF, Østerdal ML, Salvig JD,  
Mortensen LM, Rytter D, Secher NJ,  
Henriksen TB

Am J Clin Nutr, July 2008

## Conclusion

- 2.7 grams daily of LCFA in 3rd trimester may confer protection against asthma in the offspring
- This conclusion relies on the assumption that 4 grams of olive oil daily during 3rd trimester is inert in relation to asthma in the offspring

Olsen et al. Am J Clin Nutr 2008

## The Danish National Birth Cohort

Around 100,000 women  
recruited in early pregnancy  
during 1996-2002

Interviews, questionnaires,  
blood samples, registry linkages

### Plans for studies to be undertaken in the Danish National Birth Cohort

Examine the **dose-response curves** for the relation between marine n-3 fatty acids consumed in pregnancy and offspring risk of asthma

Examine if high reported intake of **olive oil**, or reporting **a Mediterranean type diet**, is associated with increased risk of asthma in the offspring

Examine interaction with other dietary factors which may have immuno-modulatory effects, such as **vitamin A, vitamin D, vitamin E, and folate**

## **Maternal marine n-3 fatty acid intake and cognitive development**

## **Maternal marine n-3 fatty acid intake and cognitive development**

Rationale that maternal intake of DHA could impact offspring neurodevelopment

- DHA has been shown to be essential to neurodevelopment in very prematurely born children (~ 32 weeks of gestation)
- DHA the most abundant fatty acid in brain
- Substantial accretion of DHA in third trimester of pregnancy

**Maternal marine n-3 fatty acid intake  
and child cognitive development**

*Still an open question whether  
maternal intake of DHA impacts  
offspring IQ*

*Do children of mothers who are  
vegetarians have lower IQ?*

.

**Maternal marine n-3 fatty acid intake  
and child cognitive development**

*Few studies, mainly*

A randomized controlled trial from Norway by  
Helland et al.

A large prospective observational study from  
Bristol by Hibbeln et al.

A study undertaken in Denmark by Oken et  
al.

## Maternal marine n-3 fatty acid intake and child cognitive development

Randomized controlled trial in Norway

590 pregnancy Norwegian women randomized

10 mL per day of cod liver oil, from gestation week 18 and the first 3 months of lactation, or corn oil placebo

90 children were examined for intelligence at 4 years

Beneficial effect of perinatal fish oil on cognitive measures

Helland et al. Paediatrics 2003

## Maternal marine n-3 fatty acid intake and child cognitive development

Randomized controlled trial in Norway

**590** pregnancy Norwegian women randomized

10 mL per day of cod liver oil, from gestation week 18 and the first 3 months of lactation

**90** children were examined for intelligence at 4 years

Beneficial effect of perinatal fish oil on cognitive measures

Helland et al. Paediatrics 2003

***Substantial attrition – and perinatal supplementation!***

## Maternal marine n-3 fatty acid intake and child cognitive development

Randomized controlled trial in Norway

590 pregnancy Norwegian women randomized

10 mL per day of cod liver oil, from gestation week 18 and the first 3 months of lactation

New follow up at 7 y where 143 children were examined

No effects detected of supplement, but association with biomarkers  
Helland et al. Paediatrics 2008

*Again substantial attrition*

## Maternal marine n-3 fatty acid intake and child cognitive development

Prospective observational study in Bristol (ALSPAC)

11875 pregnant women completed FFQ in gestation week 32

5037 children were assessed for IQ at 8 years

Seafood exposure groups: 0 g, 1-340 g, and 340 g per week

% of children with low verbal IQ declined steeply across the groups

Relation robust for adjustment for 28 potential confounders

Hibbeln et al. Lancet 2007

## Maternal marine n-3 fatty acid intake and child cognitive development

Prospective observational study in Bristol (ALSPAC)

**11875** pregnant women completed FFQ in gestation week 32

**5037** children were assessed for IQ at 8 years

Seafood exposure groups: 0 g, 1-340 g, and 340 g per week

% of children with low verbal IQ declined steeply across the groups

Relation robust for adjustment for 28 potential confounders

Hibbeln et al. Lancet 2007

*Residual confounding cannot be excluded.*

## Associations of maternal fish intake during pregnancy and breastfeeding duration with attained developmental milestones in early childhood: a study from the **Danish National Birth Cohort**

Emily Oken MD, MPH

Marie Louise Østerdal, MSc

Matthew W. Gillman MD, SM

Vibeke K. Knudsen MSc, PhD

Thorhallur I. Halldorsson MSc

Marin Strøm MScPH

David C. Bellinger ScD

Mijna Hadders-Algra MD, PhD

Kim Fleischer Michaelsen MD, Dr. Med Sci

Sjurdur F. Olsen MD, PhD

Am J Clin Nutr 2008

## Variables reflecting development

### Developmental indices assessed in 6 month postpartum interview

*13 different variables/questions*

- Total scores
- Motor scores
- Non-motor scores

### Developmental indices assessed in 18 month postpartum interview

*14 different variables/questions*

- Total scores
- Motor Scores
- Non-motor scores
  
- Age at sitting at or before 5 months
- Age at walking before 10.5 months
- Number of words greater than 60

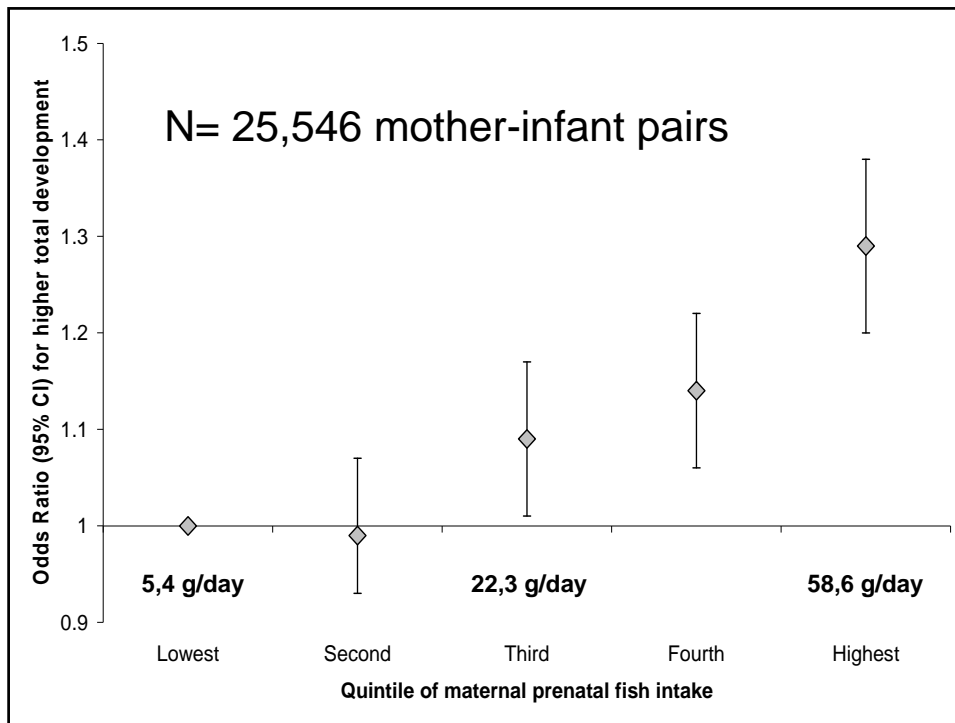
## Statistical methods

### Ordinal logistic regression

### Proportional odds model

Models the probability of obtaining a given score or higher

Allows adjustment for multiple co-variates



Ongoing study

## DHA in pregnancy and cognitive and mental function

### *Study in preparation*

- Info from registry extractions on **school performance** in Danish and foreign languages, mathematics, hard science, and social science
  - In lower secondary school (age 14-16 approx.)
  - In upper secondary school (age 16-18 approx.)

Thank you for your attention

# Arctic Food insecurity: Context and consequences

Grace Egeland



McGill



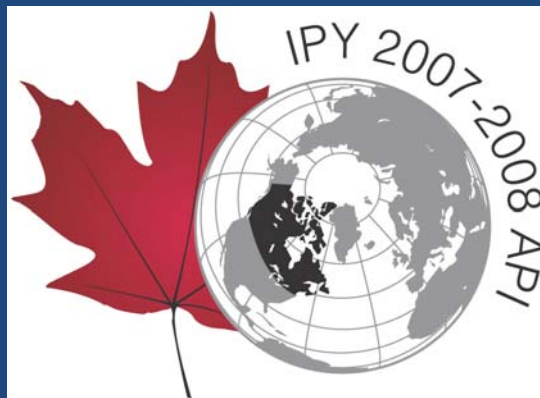
Pangnirtung Weavers' Tapestry, Pangnirtung, Baffin, Nunavut Territory

## Canadian Subsidies

Canadian subsidies for a food mail program (CAD\$46 million 2006–2007) for northern communities,

Food costs in most remote communities are at least double those in southern Canadian cities or towns closer to food distribution routes (Indian and Northern Affairs Canada, 2007).

## Canadian Federal Program for International Polar Year





## Child survey in Nunavut & Adult survey in three jurisdictions



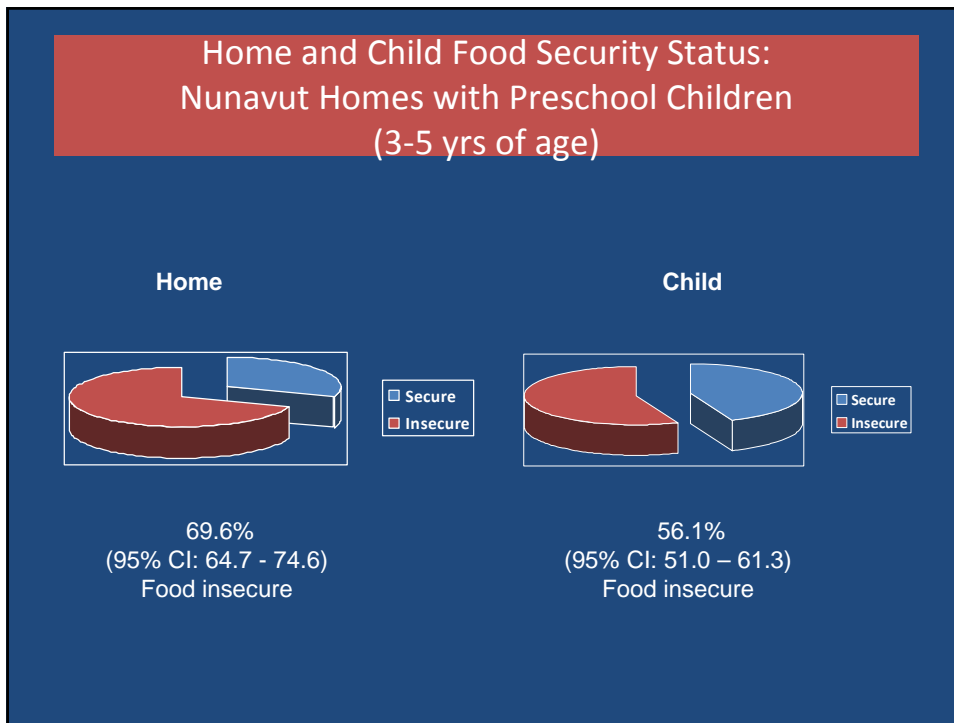
## Food Security Defined

- USDA 18-item questionnaire
- Indian and Northern Affairs Canada Modifications

### Health Canada Definitions

Food Security Status	Adults # affirmative responses/ 10	Children # affirmative responses / 8
Secure	0 – 1	0 – 1
Insecure moderate	2 - 5	2 - 4
Insecure severe	≥ 6	≥ 5





### Home and Child Food Security: Weighted Prevalence Estimates Nunavut Preschool Children (3-5 years)

	Food Security	%	(95% CI)
Home	Secure	30.4	(25.4 – 35.4)
	Insecure Moderate	35.3	(30.1 – 40.5)
	<b>Severe</b>	<b>34.3</b>	<b>(29.2 – 39.5)</b>
Child	Secure	43.9	(38.7 – 49.0)
	Insecure Moderate	31.0	(26.1 – 35.9)
	<b>Severe</b>	<b>25.1</b>	<b>(20.4 – 29.9)</b>

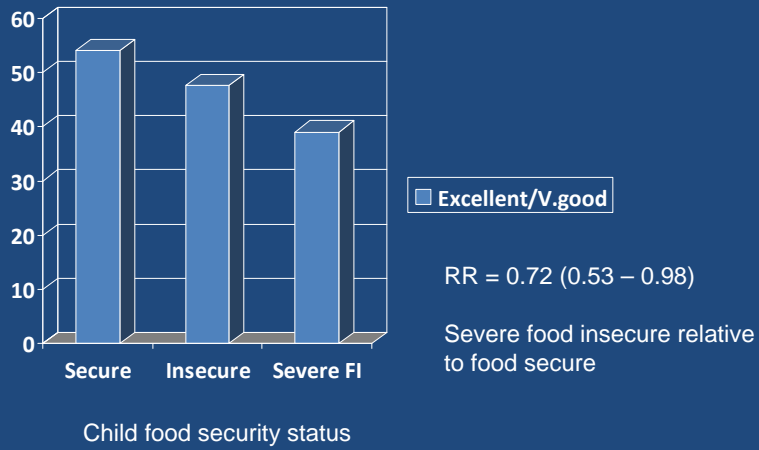
### Did the children ever skip meals because there wasn't enough money for food?

Total Prevalence:	20.3 (16.0 – 24.7)
Child	
Food Secure	0
Insecure Moderate	4.1 ( 0.4 – 7.8)
<b>Insecure Severe</b>	<b>90.4 (84.3 – 96.5)</b>

### Did your children ever not eat for a whole day because there wasn't enough money for food?

Total Prevalence:	15.3 (11.3 – 19.2)
Child	
Food Secure	0
Insecure Moderate	0.5 ( 0 - 1.5)
Insecure Severe	60.1 (49.5 - 70.7)

### Prevalence of Excellent/Good Health by Child Food Security Status

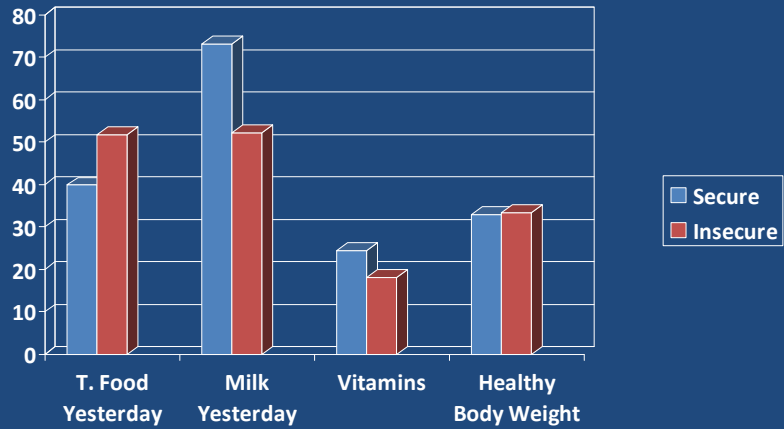


### Traditional Food (TF)

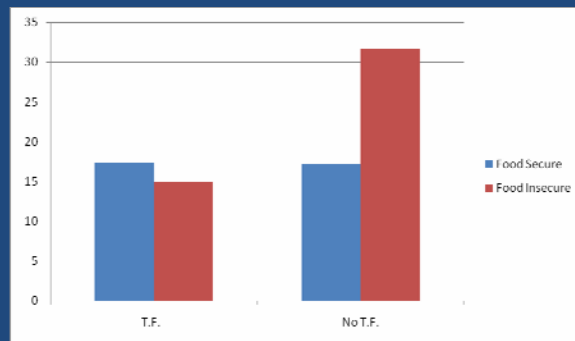


- 99% of children reported eating TF in the past month
- 46.3% reported eating TF in the past day representing a mean intake of 10.6% of energy.

### % Characteristics by Food Security Status: Nunavut Inuit Child Health Survey



### The Percent Anemic<sup>1</sup> by Past-Day Traditional Food (T.F.) Consumption (yes vs. no) and Past-year Child Food Security Inuit Nunavut Child Health Survey, 2007-2008.



<sup>1</sup>Anemia defined as a venous or capillary hemoglobin < 110 g/l for 3-4 yr olds and < 115 g/l for 5 yr olds.  $p \leq 0.10$  for the interaction term T.F. by Food Security in logistic regression model adjusting for age, sex, and sampling method (capillary vs. venous).

## Canadian Coast Guard Ship (CCGS) Amundsen



Legacy of R. Amundsen

Participatory process:

Has and is front and central to project development and ongoing utilization and communication of results;

Largest geographical area for  
a health survey

Partnerships in 3 Jurisdictions

Inuvialuit Settlement Region  
Nunavut  
Nunatsiavut

Formation of Steering  
committees

## QANUQITPIT? QANUIPPITALI? ᐱᐅᐃᐱᐸᐸ? KANUIVIT?

Inuit Health Survey 2007-2008

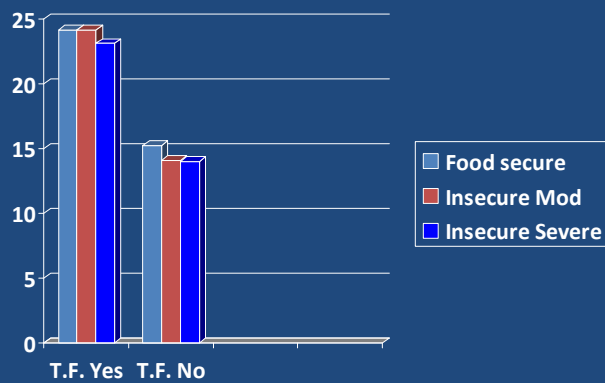


[www.inuithealthsurvey.ca](http://www.inuithealthsurvey.ca)

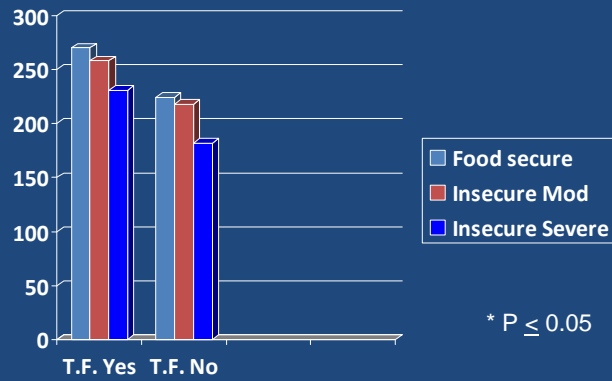


Onboard the Amundsen

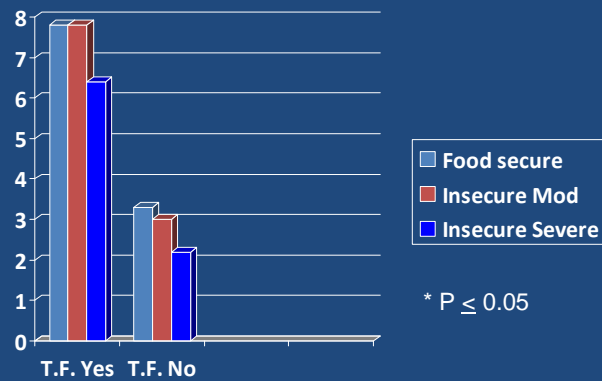
### Protein Intake (%E) by Traditional Food consumption and Food Security Status: Adult Women



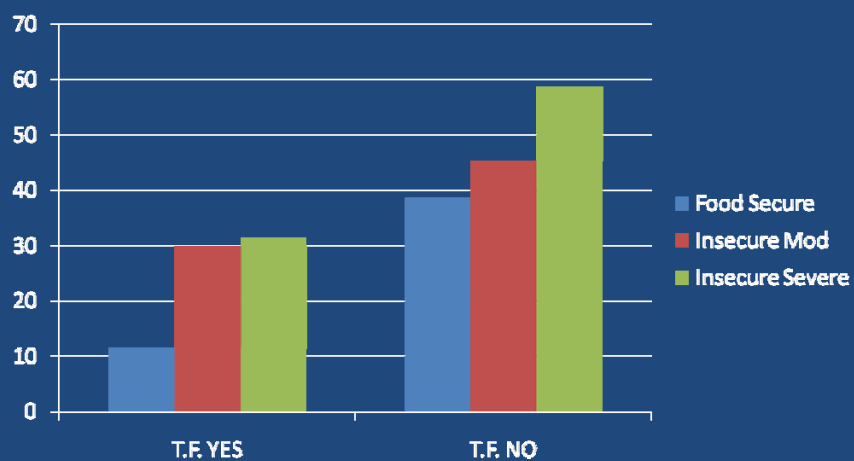
### Magnesium (mg) Intake by Traditional Food consumption and Food Security Status: Adult Women



### Vitamin D Intake (mcg) by Traditional Food consumption and Food Security Status: Adult Women

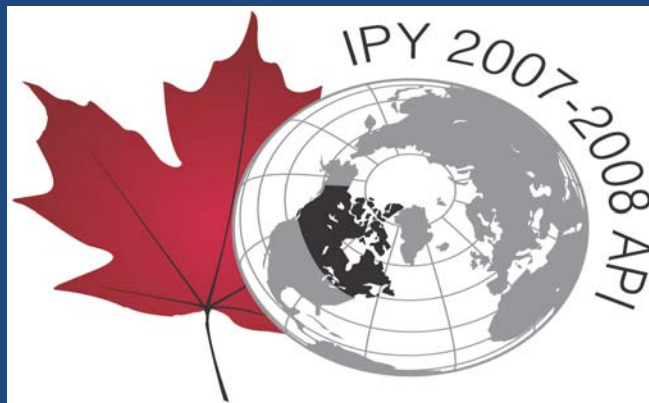


## % Low Iron stores: Men



## Past-day T.F. consumption and RBC Fatty Acids: IPY Inuit Health Survey, 207-2008

	T.F. Yes	T.F. No
<i>n</i>	1136	857
Serum 25-hydroxyvitamin D, nmol/L	55.2± 1.79	40.5± 1.79**
RBC <i>N</i> -3 fatty acids, % total fatty acids	5.90± 3.76	4.44± 2.91**
RBC Saturated fatty acids, % total fatty acids	44.7± 6.58	45.4± 7.01
RBC <i>Trans</i> -fatty acids <sup>3</sup> , % total fatty acids	1.38± 1.46	1.42± 1.48 **
<i>N</i> : <i>N</i> -3 fatty acid Ratio <sup>3</sup>	4.90± 2.08	6.69± 2.01**



Special Thanks to Canadian Federal  
Program for International Polar Year

**Taima !**





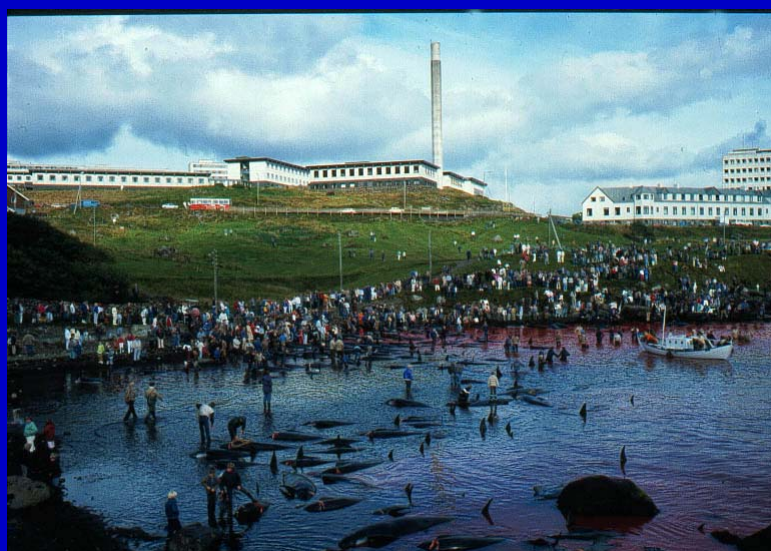
Department of Occupational  
Medicine and Public Health



## Risk versus benefits of pilot whale consumption

Pál Weihe, MD

The Faroese Hospital System  
Sigmundargøta 5, P. O. Box 14, FO-110 Tórshavn, Faroe Islands  
Tlf.: +298 31 66 96, Fax: +298 31 97 08, E-mail: [dfaa@health.fo](mailto:dfaa@health.fo)



Faroe Islands: Pilot whales are taken for food, but  
cause exposures to methylmercury, PCB, etc.


## Why whales concentrate pollutants

Long-lived and large, but accumulation of pollutants depends on food:

- 1) Baleen whales: feed on plankton and fish low in the food chains – less pollution
- 2) Toothed whales: feed on larger fish and squid higher up in the food chains - more pollution


## Whale contaminants – Human health concerns

- Mercury (methylmercury)
- Persistent organic pollutants (POPs):
  - Pesticides (DDT, Toxaphene, etc.)
  - Polychlorinated biphenyls (PCBs)
  - Other industrial chemicals (HCB, etc.)
  - Maritime pollutants (organotins, etc.)

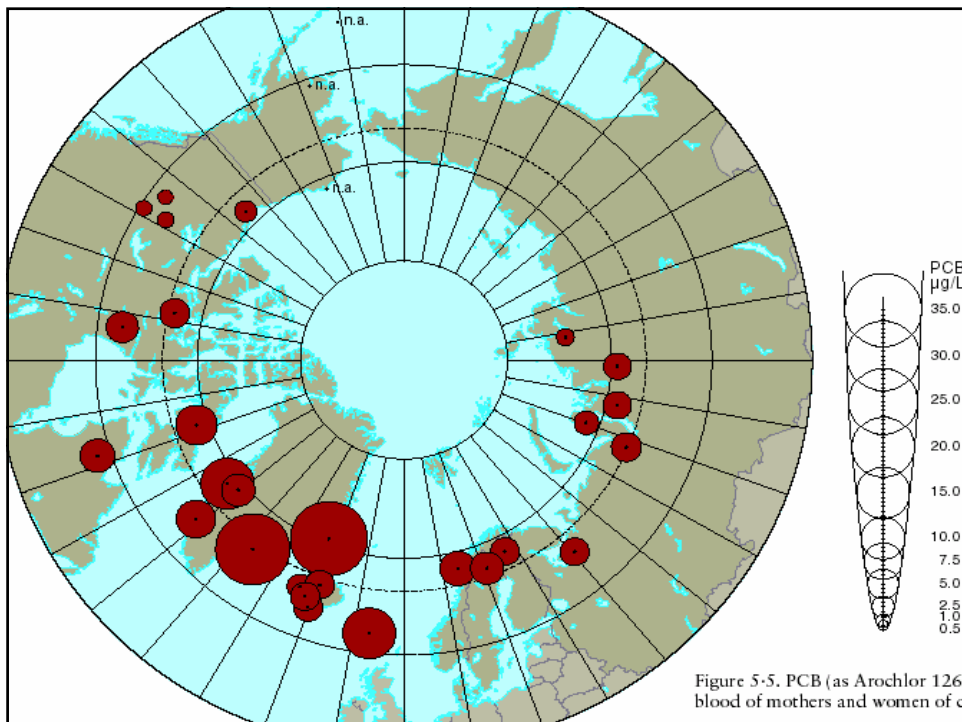
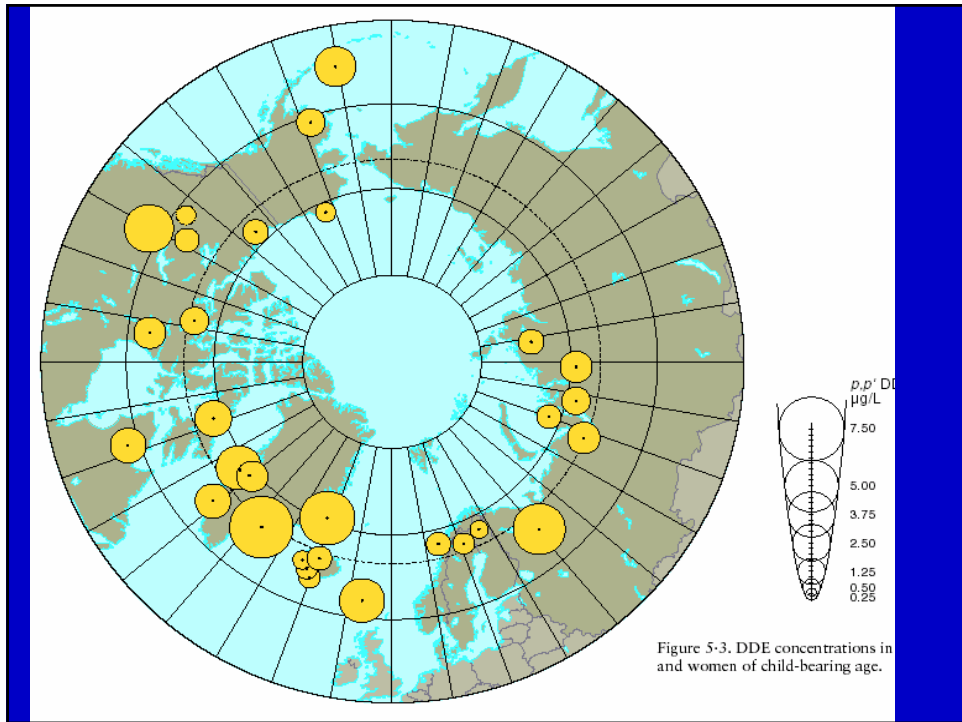


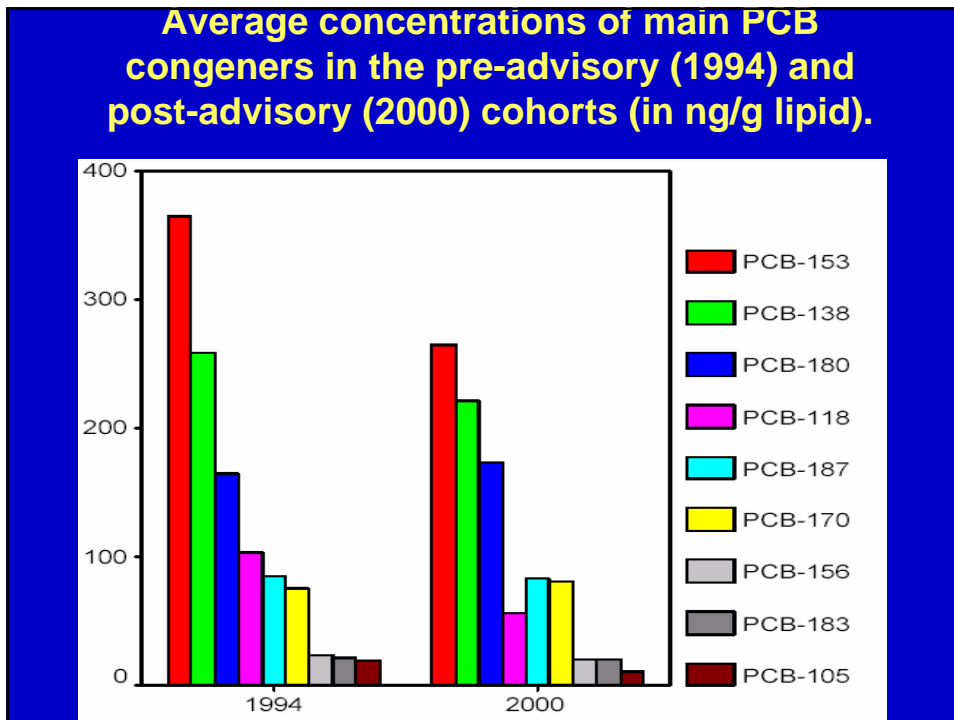
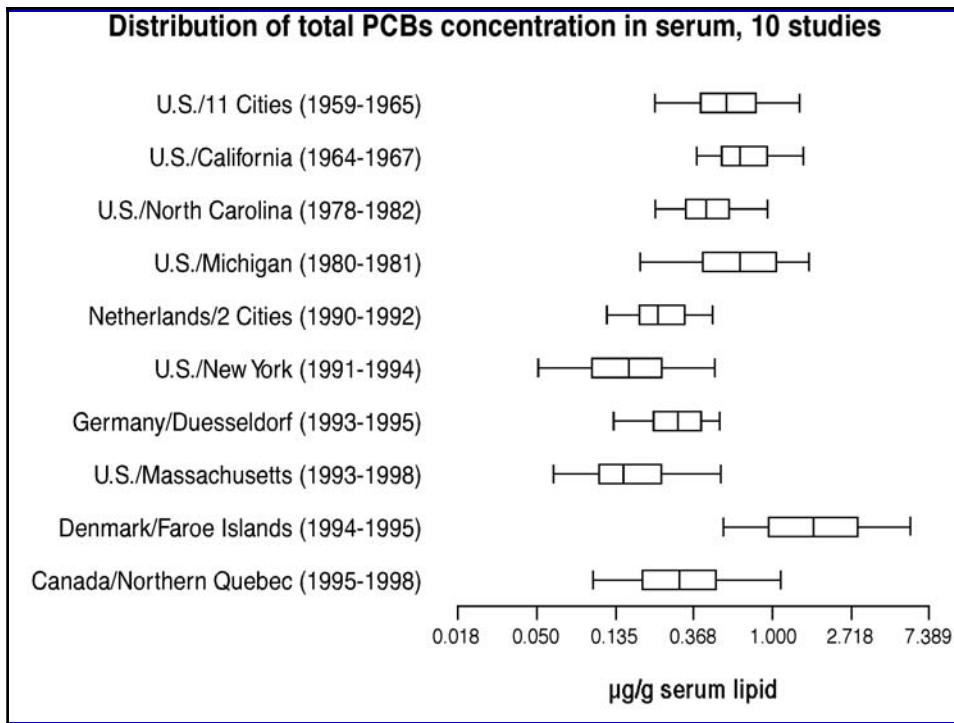
Pilot whale intake causes mixed exposures:  
Methylmercury from meat,  
PCBs from blubber -  
Meat and blubber intakes vary independently

**AMAP Assessment 2002:**  
Human Health in the Arctic



Arctic Monitoring and Assessment Programme (AMAP)





## Maternal serum

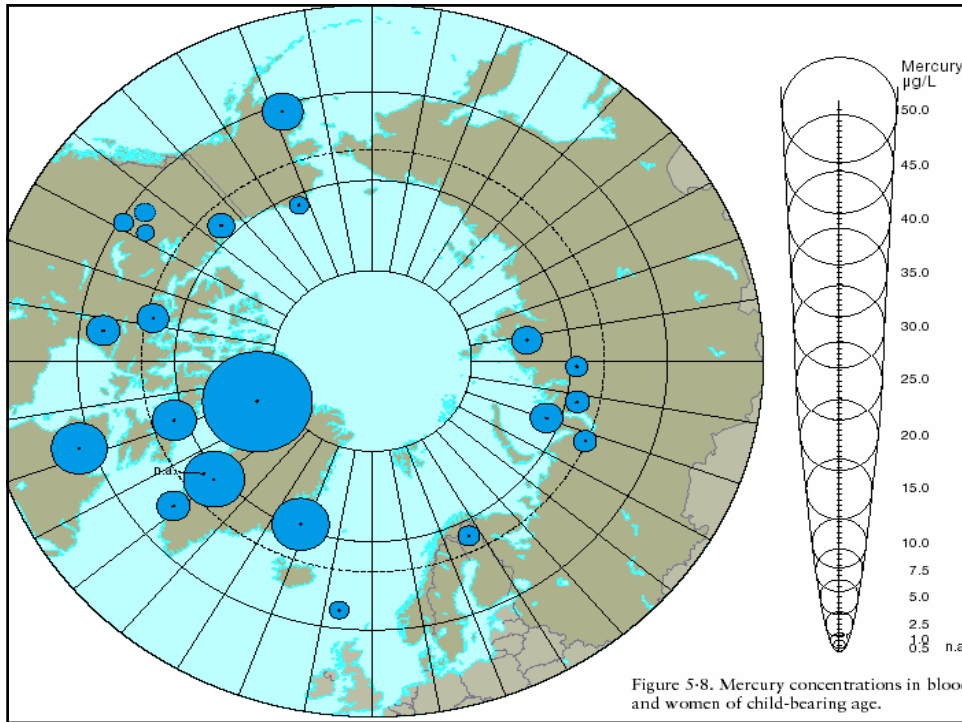
Cohorts (year)	n	Geometric mean sumPCB* (range) $\mu\text{g/g}$ lipid	Geometric mean DDE (range) $\mu\text{g/g}$ lipid
Cohort 2 (1994-1995)	173	1.12 (0.04-18.4)	0.72 (0.18-8.0)
Cohort 3 (1998-2000)	464	1.25 (0.83-1.90)	0.60 (0.06-11.35)**
Cohort 5 (2007-2009)	501	0.42 (0.02-3.00)	0.13 (0.01-1.52)

\*sumPCB=(PCB 138+153+180)\*2

\*\* in milk, n=600

## Septuagenarians – 2008/9

Substance	n	Mean (range) $\mu\text{g/g}$	Median $\mu\text{g/g}$
SumPCB (lipid)	489	1.76 (0.08-17.6)	1.32
Hair	611	3.1 (0.02-32.7)	2.2



*Total mercury in umbilical cord blood in Faroese cohorts in µg/l*

Cohort	Year	N	Geometric mean	Min.	Max.
Cohort 1	1986-87	894	22.9	0.90	351
Cohort 2	1994	163	20.9	1.90	102
Cohort 3	1998 -2000	603	12.3	1.60	193
Cohort 4 (mother-serum)	2000-2001	148	1,86	.001	7.50
Cohort 5	2007-2009	490	3.01	0.25	37.6

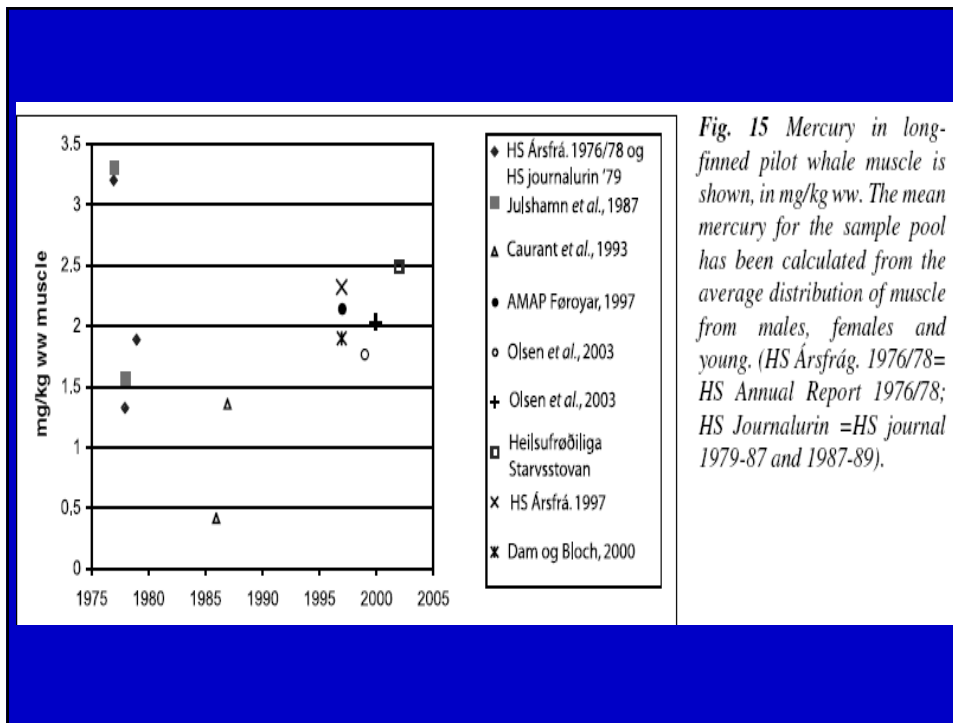


Fig. 15 Mercury in long-finned pilot whale muscle is shown, in mg/kg ww. The mean mercury for the sample pool has been calculated from the average distribution of muscle from males, females and young. (HS Ársfrág. 1976/78= HS Annual Report 1976/78; HS Journalurin =HS journal 1979-87 and 1987-89).

## Mercury in cod wet weight in $\mu\text{g/g}$

- 1977/78: 0,03 (N= 557)
- 1994: 0,01 (N= 25)
- 1997: 0,03 (N= 44)
- 2000: 0,02 (N = 49)
- 2001: 0,02 (N = 25)

## Mercury in haddock wet weight in $\mu\text{g/g}$

- 2001:  $< 0,012$  (N=25)

AMAP Faroe Islands Heavy metals and POPs core  
programme 2005-2008  
Katrín Hoydal and María Dam, Environment Agency, Faroe  
Islands, Report no. US 2009:1

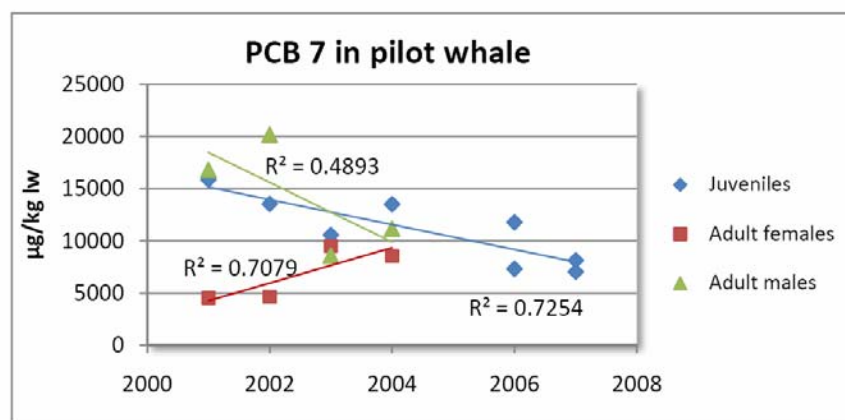
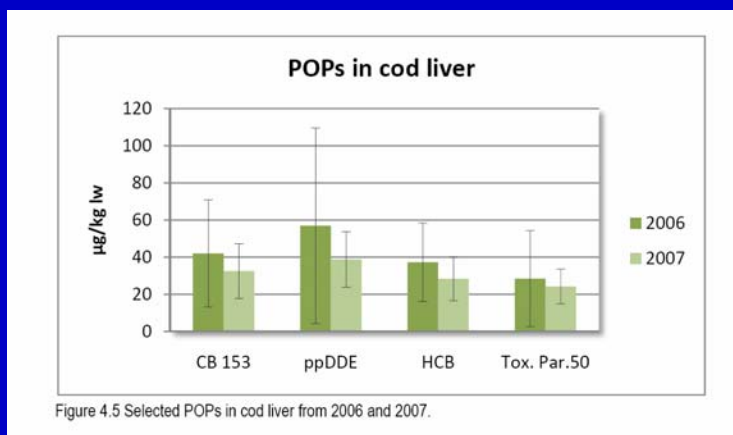


Figure 4.7 PCB 7 in pilot whale blubber from 2001 to 2007

AMAP Faroe Islands Heavy metals and POPs core programme 2005-2008  
 Katrin Hoydal and Maria Dam, Environment Agency, Faroe Islands,  
 Report no. US 2009:1



## Faroese Diet 1981-82

### daily average intake per person

Source: Vestergaard & Zachariassen, Fróðskaparrit 1987

- Milk products: 390 g
- Meat: 68 g
- Fish: 72 g
- Vegetables: 224 g
- Bread: 215
- Meat from pilot whales: 12 g
- Blubber from pilot whales: 7 g

**Faroese Diet 2000-2001**  
**daily average intake per person**  
**(pregnant women)**

- Milk products: 517 g
- Meat: 155 g
- Fish: 38 g
- Vegetables: 272 g
- Bread: 323
- Meat from pilot whales: 1,4 g
- Blubber from pilot whales: 0,6 g

**Warning signal on mercury from Japan:**

*...in every case the mother was healthy,  
and it was not until more than three months after  
birth that the symptoms were recognised*  
(Kitamura, 1959)



### *Methylmercury*: Early observations of developmental toxicity

1952	Developmental neurotoxicity in two infants (Sweden)
1968	Minamata disease causation formally recognised (Japan)
1972	Rodent experiments show delayed developmental neurotoxicity (USA)
1986	Adverse effects observed in children from maternal fish intake during pregnancy (New Zealand)

**Several major epidemiological studies have been performed since this recommendation in:**

- New Zealand
- Seychelles Islands
- The Faroe Islands

All three well-designed, prospective studies that have examined the effects of prenatal exposure to low dose of methylmercury

### Main differences between three major prospective studies of methylmercury-exposed children

Attribute	New Zealand	Faroes	Seychelles
Source of exposure	Shark and ocean fish	Whale, ocean fish and shellfish	Ocean fish
Mercury exposure assessment	Maternal hair	Cord blood, cord tissue, and maternal hair	Maternal hair
Mercury effect	Significant	Significant	Not significant
Effect of maternal fish intake	Mothers were matched for high fish intake	Adjustment for maternal fish intake increased mercury effect	Maternal fish intake not included in data analysis
Other toxicant exposures	Lead in house paint and air	PCBs (whale blubber)	Tropical pesticide use
Language	English (and Pacific languages)	Faroese (and Danish)	Creole (English and French)
Socioeconomic setting	Industrialized Western	Industrialized Scandinavian	Middle-income developing
Family-setting	Urban, mixed cultures	Traditional	Mainly matriarchal
Outcome tests	Omnibus	Domain-related and neurophysiological	Omnibus and domain-related
Clinical examiners	Clinical specialists	Clinical specialists	Nurse/student

In 1990 the WHO expert committee stated:

“There is a need for epidemiological studies on children exposed *in utero* to levels of methylmercury that result in peak maternal hair mercury levels below 20 µg/g, in order to screen for those effects only detectable by available psychological and behavioural tests”.

Scientific committees under both WHO and under the US National Research Council recently have reviewed the findings of these studies. However, they conclude differently, as can be seen in the following extracts from the conclusions.

**Committee on the Toxicological Effects of Methylmercury, Board on Environmental Studies and Toxicology, US-National Research Council concluded in 2000:**

“On the basis of its evaluation, the committee’s consensus is that the value of US-EPA’s current Reference Dose (RfD) for MeHg, 0,1 µg/kg per day, is a scientifically justifiable level for the protection of public health. However, the committee recommends that the Iraqi study no longer be used as the scientific basis of the RfD. The RfD should still be based on the developmental neurotoxic effects of MeHg, but the Faroe Islands study should be used as the critical study for the derivation of the RfD. “

**Committee on the Toxicological Effects of Methylmercury, Board on Environmental Studies and Toxicology, US-National Research Council concluded in 2000:**

Based on cord blood analyses from the Faroe Islands study, the lowest BMD (Benchmark Dose) for a neurobehavioral end point the committee considered to be sufficiently reliable is for the Boston Naming Test.

That approach estimates a BMDL (BMD lower confidence limit) of 58 ppb of Hg in cord blood (corresponding to a BMDL of 12 ppm of Hg in hair) as a reasonable point of departure for deriving a RfD.

A safety factor of 10 leads to a limit value in hair of only 1,2 ppm. This value not only some of the arctic populations will exceed, e.g. in Greenland and the Faroes, but even non-arctic areas.

1,2 ppm in hair corresponds to an intake of 0,1 µg per kg body weight per day (RfD - Reference Dose)

## NRC exposure limit calculated from the benchmark dose (and our update)

Mercury concentrations	NRC	Updated
BMDL ( $\mu\text{g/L}$ cord blood)	58	43 <sup>+</sup>
Cord blood adjustment (1.5 <sup>*</sup> )	-	29
Uncertainty factor	(10)	(10)
Exposure limit ( $\mu\text{g/L}$ blood)	5.8	2.9
Converted to $\mu\text{g/kg}\cdot\text{d}$	0.1	0.05

EPA RID

BMDL:  $P_0 = 0.05$ , BMR = 0.05, linear slope for BNT

<sup>+</sup>Adjusted for exposure assessment imprecision by SEM

<sup>\*</sup>Based on hair-to-blood ratios in pregnant and non-pregnant subjects

### The Joint FAO / WHO Expert Committee on Food Additives (JECFA) concluded in 2000 the following on limits values to mercury exposure:

“The studies in the Faroe Islands and the Seychelles that were evaluated by the Committee did not provide consistent evidence of neurodevelopmental effects in children of mothers whose intake of methylmercury yielded hair burdens of 20  $\mu\text{g/g}$  or less. The Committee could not evaluate the risks for the complex and subtle neurological end-points used in these studies that would be associated with lower intakes. In the absence of any clear indication of a consistent risk in these recent studies, the Committee decided to maintain the PTWI of 3.3  $\mu\text{g/kg}$  and recommended that methylmercury be re-evaluated in 2002, when the 96-month evaluation of the Seychelles cohort and other relevant data that may become available can be considered. “

**JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES**  
**Sixty-first meeting**  
**Rome, 10-19 June 2003**

A steady-state intake of 1.5 µg methylmercury/kg bw/day was estimated to represent the exposure that would be expected to be without appreciable adverse effects in children. A total factor of 6.4 (2 x 3.2) was applied to this figure to derive a PTWI of 1.6 µg/kg bw. This PTWI is considered sufficient to protect the developing fetus, the most sensitive subgroup of the population.

### *Dose-response assessments*

**Table: Estimates of maternal hair concentrations associated with the NOEL/BMDL for neurotoxicity associated with in utero exposure**

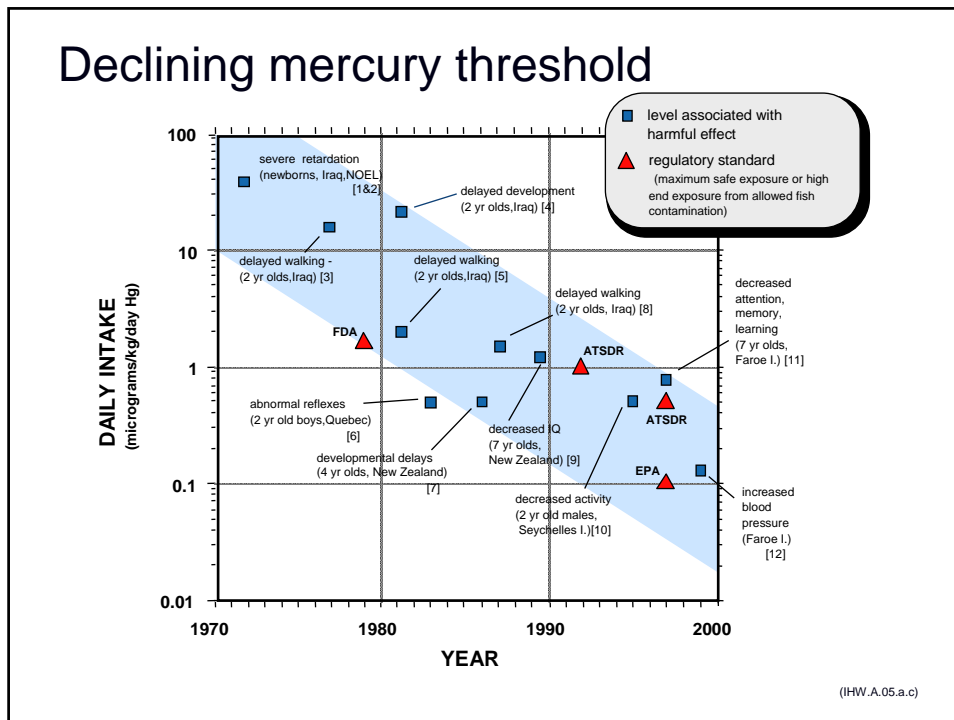
Study	N	NOEL/ BMDL
Faroes	917	12 mg/kg maternal hair <sup>1</sup>
Seychelles	711	15.3 mg/kg maternal hair <sup>2</sup>
Composite		14 mg/kg maternal hair

<sup>1</sup> Budtz-Jorgensen et al., 1999, 2000, 2001; U.S. National Research Council, 2000; Rice et al., 2003

<sup>2</sup> U.S. ATSDR, 1999

The maternal hair-mercury concentration corresponding to a no observed effect level (NOEL) for neurobehavioural effects was identified for the Seychelles Islands study, and a mathematical analysis of the concentration-response relationship was used to determine a benchmark dose lower confidence limit (BMDL) for the Faroos Islands and New Zealand studies. The Committee noted that one child (of the 237) in the New Zealand study sample had a large impact on the BMDLs. The maternal hair-mercury level for this child was 86 mg/kg, more than four times the next highest maternal-hair mercury level in the study sample. Including this observation produced BMDLs of 17 to 24 mg/kg, while omitting it produced BMDLs of 7.4 to 10 mg/kg. Because of uncertainty about which set of BMDLs is most valid, the Committee decided to base the evaluation only on the Faroos Islands and Seychelles Islands studies. The Committee noted, however, that including the New Zealand study did not materially alter the conclusions of the evaluation.

The Committee used the average from the two studies, 14 mg/kg maternal hair-mercury, as an estimate of the level in maternal hair reflecting exposures that would be without appreciable adverse effects in the offspring in these two study populations.



## Faroese birth cohort studies

- Total of ~2,500 mother-child pairs
- Focus on methylmercury
- Maternal exposure during pregnancy
- Neurobehavioral development
- Blood pressure and growth
- Endocrine function
- Immune function

## How we have measured neurodevelopment in the Faroes

- Neuropsychological methods
- Neurophysiological methods
- Neuropediatric methods

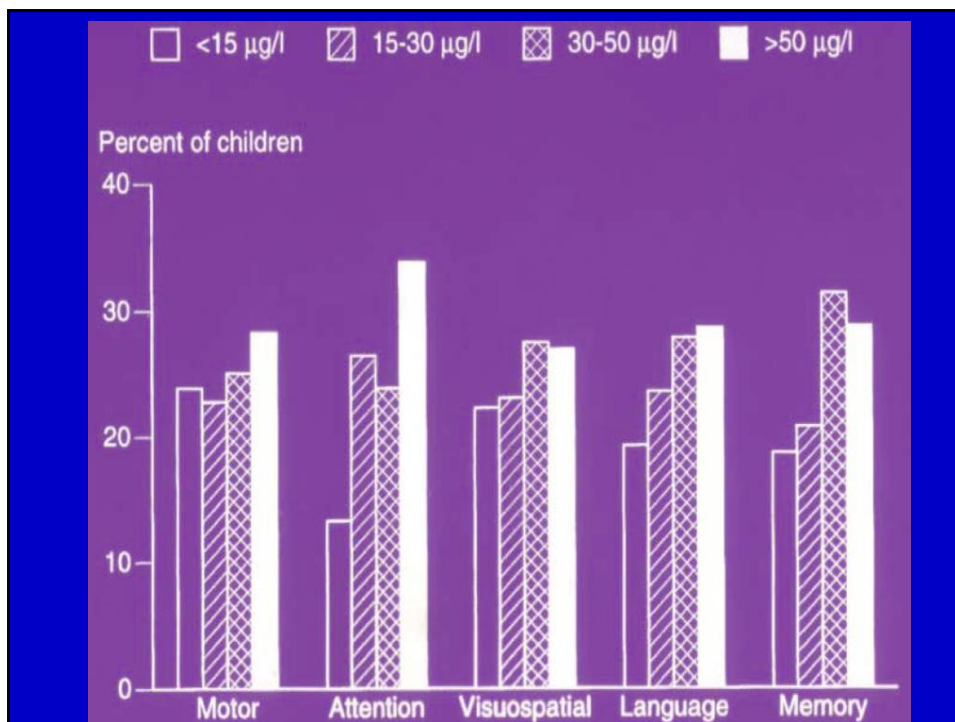
## Neuro-Psychological Domains

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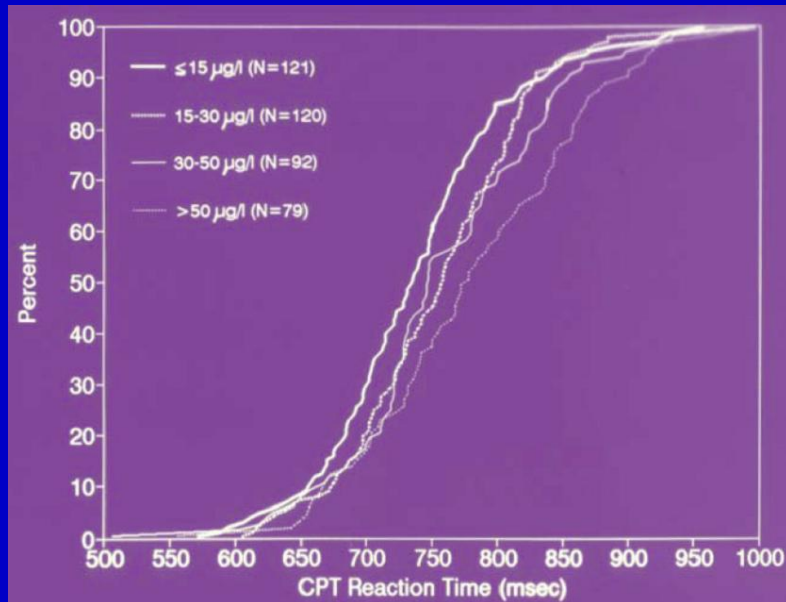
- Learning and memory:
  - Verbal material
  - Visuospatial material
  - Learning
  - Short Term Memory
  - Long Term Memory
  - Recognition

## Neuro-Psychological Domains

- Visuo-Constructive Abilities
- Fine Manual-Motoric function
- Visuo-Motoric Coordination
- Aquisition of Language and Vocabulary
- Verbal Abstraction (concepts)
- Attention and Concentration
  - selective
  - sustained
- Visuo-Motoric Speed



## NES – Reaction Time, Age 7



### Mercury effect as developmental delay (months at age 7 years) for each doubling of exposure

Motor (Finger tapping, PH)	0.9
Attention (CPT-reaction time)	1.3
Visuospatial (Bender errors)	0.6
Language (Boston Naming)	1.6
Verbal memory (CVLT short delay)	2.0

## P values for PCB (and Hg) after adjustment for Hg

Test*	PCB	Hg
CPT-reaction time	0.67	0.002
Boston Naming	0.27	0.06
CVLT long delay	0.64	0.08

\* where PCB (alone) is significant

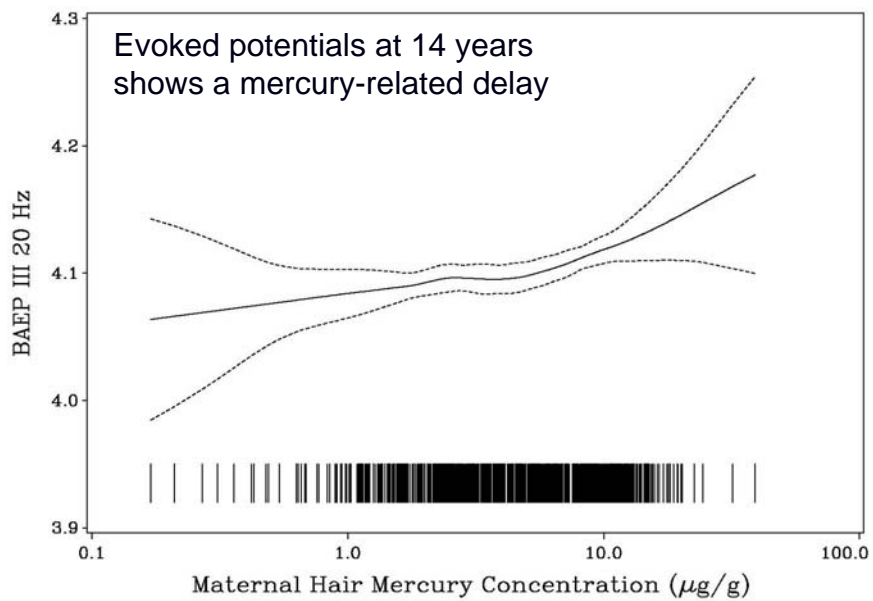
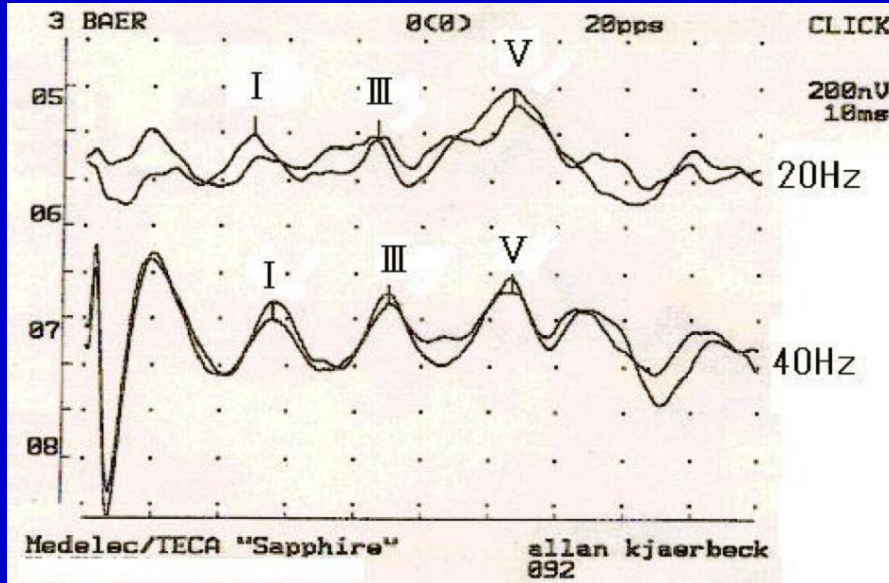
## Betas for PCB in Hg exposure tertile groups

Test*	I	II	III
CPT-reaction time	-6.6	2.8	38.4
Boston Naming	-1.0	-0.6	-1.6
CVLT long delay	-0.2	-0.1	-0.9

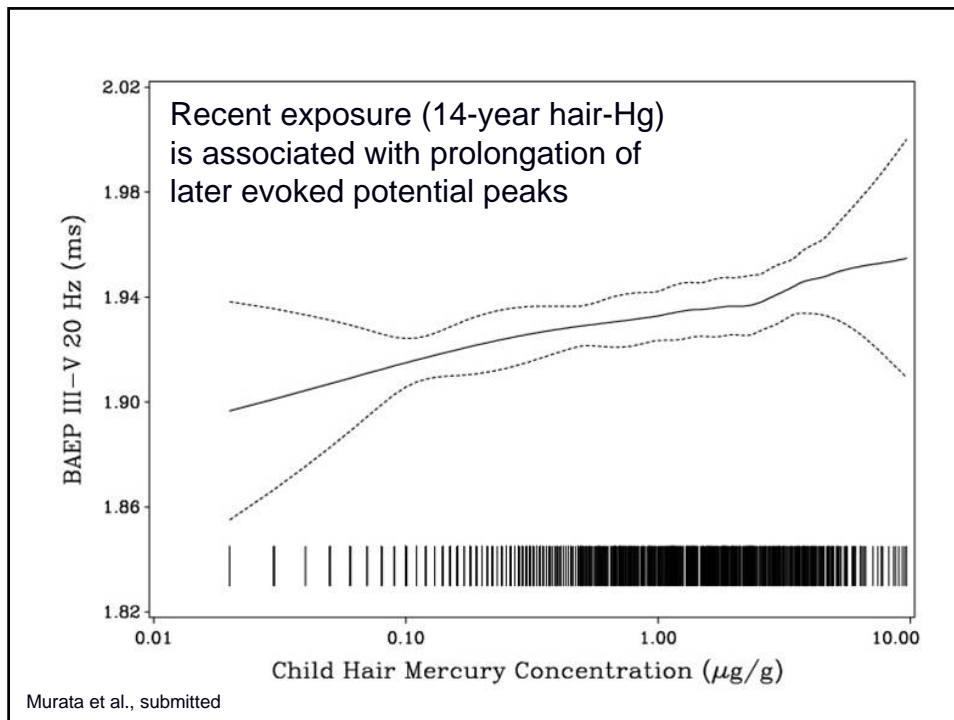
\* where PCB (alone) is significant



## Brainstem auditory evoked potentials

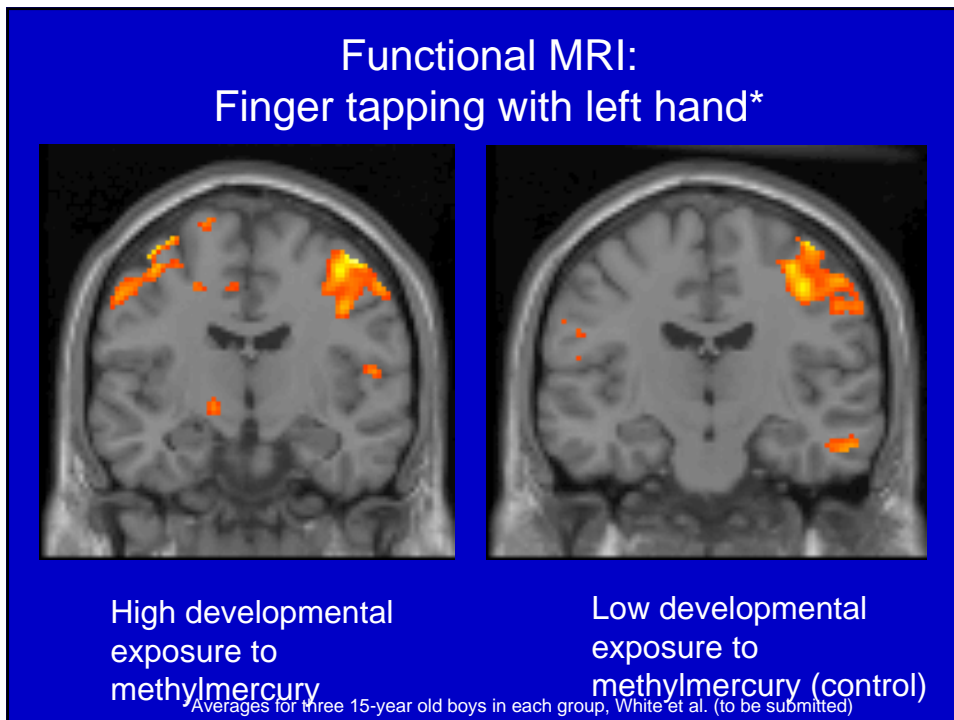
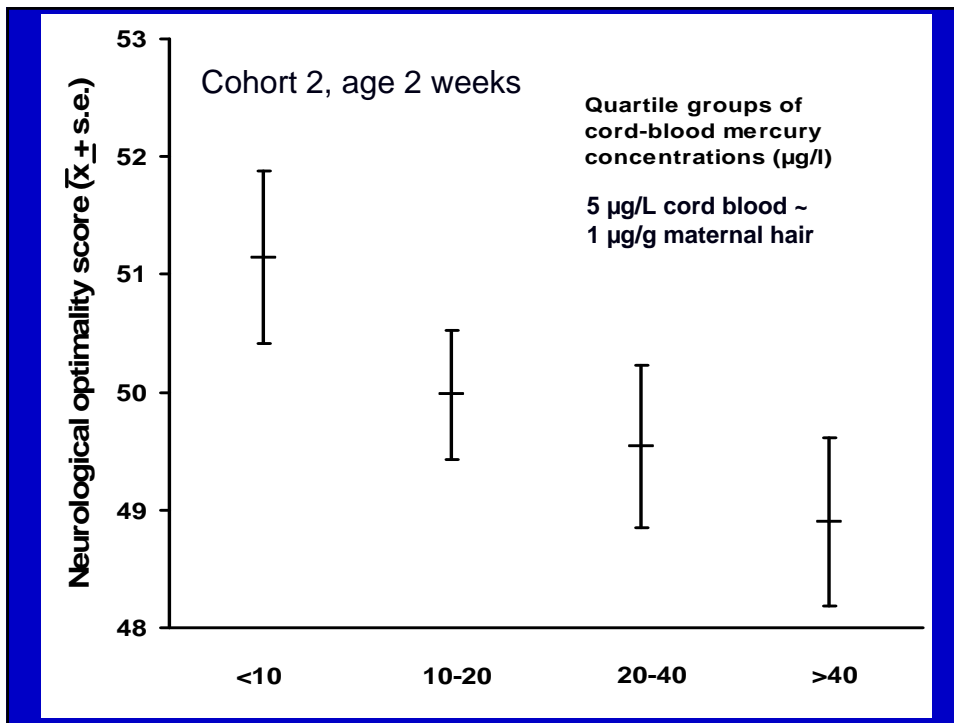


Murata et al., submitted



## Neurological Optimality Score (NOS)

The Groningen Neonatal Neurological Examination records systematically main neurological functions, such as posture, motility, movements, tonus, responses, tendon reflexes, other reactions, reactivity, and stability of behavioral status during the examination. The technique for the examination of the children is a comprehensive age-adequate examination as described by Prechtl (Prechtl, 1977).



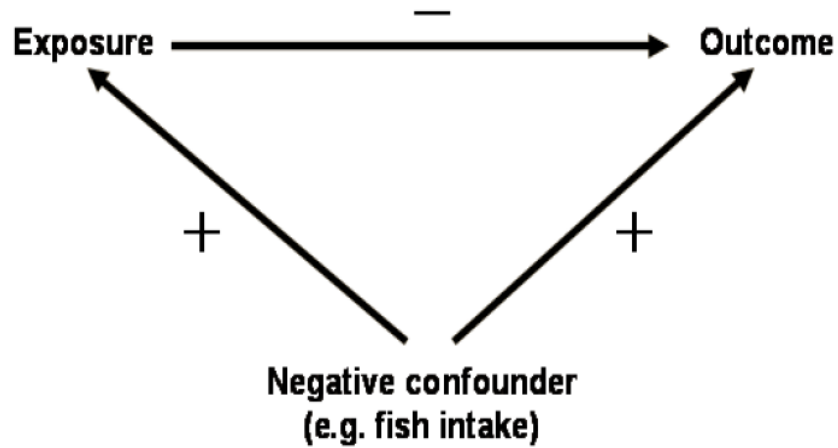
## Conclusions on developmental neurotoxicity related to MeHg

- Neurobehavioral effects most clearly on attention, memory and language, but also visuospatial and motor functions
- Parallel neurophysiological findings
- Prenatal generally more toxic than early postnatal exposure
- Results from age 14 years suggest that effects are permanent

## Underestimation of a mercury effect needs consideration

- Imprecise exposure assessment
- Protective nutrients in seafood
- Imprecise outcome measures
  - Psychometric test properties
  - Test administration
- Overadjustment for confounders?
- Two-sided p-values and limited power

**Negative confounding: fish intake (a negative confounder) is positively associated with both methylmercury (exposure) and neurodevelopment or cardiovascular health (outcome), and the exposure has adverse effects on the outcome. Failure to adjust for fish intake would result in underestimation of both mercury toxicity and fish benefits**



**Examples of potential negative confounders associated with corresponding exposure sources and toxic hazards**

Exposure sources	Toxic hazards	Potential negative confounders
Freshwater fish, seafood	Methylmercury, PCBs, dioxins	Fish oil, vitamins, trace elements
Fruits and nuts	Aflatoxin, pesticide residues	Vitamins, antioxidants
Vegetables	Nitrate	Anticarcinogens
Red meat	Beef hormones, contaminants	Complete proteins
Artificial sweeteners	Possible carcinogens	Caloric restriction
Breast-feeding	Maternal lipophilic drugs, pollutants	Essential nutrients, antibodies, psychological benefits
Occupation	Hazards at work	Benefits from being employed

W-179

## Underestimation of adverse effects of mercury exposure unadjusted for beneficial effects of seafood consumption

Esben Budtz-Jørgensen<sup>1,\*</sup>, Pal Weihe<sup>2</sup>, Philippe Grandjean<sup>3,4</sup>

<sup>1</sup>Department of Biostatistics, University of Copenhagen, Denmark; <sup>2</sup>Department of Occupational and Environmental Health, The Faroese Hospital System, Torshavn, Faroe Islands; <sup>3</sup>Department of Environmental Medicine, Institute of Public Health, University of Southern Denmark, Denmark; <sup>4</sup>Department of Environmental Health, Harvard School of Public Health, Boston, USA \*Email: ebj@biostat.ku.dk

### Background

Methylmercury is a common contaminant of seafood and occurs in varying concentrations in different types of seafood, which also contain essential nutrients. Subjects exposed to methylmercury from their diet are therefore likely to differ in regard to intake of nutrients which may have beneficial effects that could perhaps compensate for the toxic effects of mercury. We have examined this issue in a birth cohort from the Faroe Islands.

### The Faroese Mercury Study

### Bias due to confounder imprecision

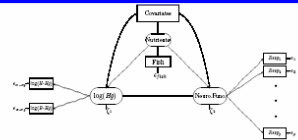
In a regression model with exposure  $X$  and true confounder  $Z$ :  $Y = \beta_0 + \beta_1 X + \beta_2 Z + \epsilon$ , if the observed confounder  $V$  has additive error  $V = Z + U$  and  $Z$  is naively replaced by  $V$  in the analysis, then the exposure effect estimate is affected by an additive bias term, i.e.,

$$\hat{\beta}_2 \rightarrow \beta_2 + \beta_1 \cdot [\text{cov}(X, Z) / \text{var}(X)] - [\text{var}(U) / \text{var}(V) X]$$

In the case where  $X$  is mercury exposure and  $Z$  nutrients from fish, the effect of  $Z$  on  $Y$  ( $\beta_2$ ) is positive and so is the covariance between mercury exposure and nutrients intake  $\text{cov}(X, Z)$ . Therefore, the bias term is

Without mutual adjustment for beneficial and toxic effects, and without allowance for imprecision, the opposite effects of mercury and nutrient intakes from seafood are underestimated. Assessment of adverse effects caused by toxicants therefore needs to adjust for both confounding and imprecision of the exposure variables.

... mercury concentrations in cord blood and maternal hair were assumed to be manifestations of an underlying true exposure. Similarly, outcome variables were grouped into motor functions and verbally-mediated functions that were each joined into a latent variable [3]. Tests conducted at 14 years were also split into groups. The latent exposure and potential confounders were assumed to affect each of the latent outcome functions [2]. Frequency of maternal fish dinners was added as a separate covariate (Figure 1).



### Mercury effects on neurobehavioral tests at 7 and 14 years of age, as determined in structural equation analysis with covariate adjustment before and after addition of the frequency of maternal fish dinners during pregnancy (Budtz-Jørgensen et al., 2007)

Age/test group	Mercury without adjustment for fish intake		Mutual adjustment			
	Effect	p-Value	Fish intake		Mercury	
	Effect	p-Value	Effect	p-Value	Effect	p-value
7 years						
Motor	-9.74	0.034	25.1	0.010	-12.2	0.0092
Verbal	-10.4	0.0018	3.62	0.61	-10.8	0.0017
14 years						
Motor	-7.41	0.033	19.9	0.006	-9.37	0.0082
Attention	-8.40	0.029	12.2	0.13	-9.54	0.016
Spatial	2.60	0.50	17.3	0.031	1.04	0.79
Verbal	-5.97	0.080	9.85	0.16	-6.87	0.049
Memory	-2.86	0.39	3.15	0.64	-3.05	0.37

## Exposure Parameters

	<u>Geometric Mean</u>	<u>Interquartile Range</u>
Cohort 1		
cord blood Hg (nmol/L)	114.3	67.0-207.3
cord blood Se (nmol/L)	1412.5	1276-1558
Hg/Se molar ratio	0.08	0.05 – 0.15
Cohort 2		
cord blood Hg (nmol/L)	104.7	62.4-200.0
cord blood Se (nmol/L)	1288	1180-1418
Hg/Se molar ratio	0.08	0.05 – 0.14

## Assessing Hg and Se Interactions

Outcome = f (Hg, Se, Hg\*Se, covariates )

Hg\*Se interaction:

- Hg by low, medium, and high Hg/Se ratio (25% lowest, 50%, and 25% highest of ratio distribution)

## Mercury associated effects at 7 years - Cohort 1

	Hg/Se ratio			Hg
	Q1	Q2-Q3	Q4	All <sup>a</sup>
Finger Tapping preferred hand	-	↑	↓	↓
CPT avg. reaction time (ms)	-	-	↓	↓*
Bender errors	↓	-	-	↓
BNT total correct after cues	↓	↓	↓	↓*
CVLT long delay	-	-	↑	↓

Improvement

↑ 0.10 &lt; p &lt; 0.30

↑↑ 0.05 ≤ p ≤ 0.10

Deficit

↓ 0.10 &lt; p &lt; 0.30

↓↓ 0.05 ≤ p ≤ 0.10

<sup>a</sup>Grandjean et al. 1997  
Neurotoxicol and Teratol  
19:417-428.

## Conclusion

- On the average, Se was present in cord blood in a molar excess of about 10-fold above Hg
- Se concentrations suggested all children were Se sufficient
- No evidence that Se was a significant protective factor against MeHg neurotoxicity
- Selenium intake can therefore not explain the significant benefits associated with fish intake
- Preventive methods are needed to address MeHg exposures, rather than Se intakes, while maintaining a high fish/seafood intake

### Separation of Risks and Benefits of Seafood Intake

*Esben Budtz-Jørgensen,<sup>1</sup> Philippe Grandjean,<sup>2,3</sup> and Pal Weihe<sup>2,4</sup>*

**RESULTS:** Adjustment for the benefits conferred by maternal fish intake during pregnancy resulted in an increased effect of the prenatal methylmercury exposure, as compared with the unadjusted results. The dietary questionnaire response is likely to be an imprecise proxy for the transfer of seafood nutrients to the fetus, and this imprecision may bias the confounder-adjusted mercury effect estimate. We explored the magnitude of this bias in sensitivity analysis assuming a range of error variances. At realistic imprecision levels, mercury-associated deficits increased by up to 2-fold when compared with the unadjusted effects.

**CONCLUSIONS:** These results suggest that uncontrolled confounding from a beneficial parameter, and imprecision of this confounder, may cause substantial underestimation of the effects of a toxic exposure. The adverse effects of methylmercury exposure from fish and seafood are therefore likely to be underestimated by unadjusted results from observational studies, and the extent of this bias will be study dependent.

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### Mercury effects on neurobehavioral tests at 7 and 14 years of age, as determined in structural equation analysis with covariate adjustment before and after addition of the frequency of maternal fish dinners during pregnancy (Budtz-Jørgensen et al., 2007).

Age/test group	Mercury without adjustment for fish intake		Mutual adjustment			
	Effect	p-Value	Fish intake		Mercury	
	Effect	p-Value	Effect	p-Value	Effect	p-value
7 years						
Motor	-9.74	0.034	25.1	0.010	-12.2	0.0092
Verbal	-10.4	0.0018	3.62	0.61	-10.8	0.0017
14 years						
Motor	-7.41	0.033	19.9	0.006	-9.37	0.0082
Attention	-8.40	0.029	12.2	0.13	-9.54	0.016
Spatial	2.60	0.50	17.3	0.031	1.04	0.79
Verbal	-5.97	0.080	9.85	0.16	-6.87	0.049
Memory	-2.86	0.39	3.15	0.64	-3.05	0.37

## Exposure Parameters

	<u>Geometric Mean</u>	<u>Interquartile Range</u>
Cohort 1		
cord blood Hg (nmol/L)	114.3	67.0-207.3
cord blood Se (nmol/L)	1412.5	1276-1558
Hg/Se molar ratio	0.08	0.05 – 0.15
Cohort 2		
cord blood Hg (nmol/L)	104.7	62.4-200.0
cord blood Se (nmol/L)	1288	1180-1418
Hg/Se molar ratio	0.08	0.05 – 0.14

## Assessing Hg and Se Interactions

Outcome = f (Hg, Se, Hg\*Se, covariates )

Hg\*Se interaction:

- Hg by low, medium, and high Hg/Se ratio (25% lowest, 50%, and 25% highest of ratio distribution)

## Mercury associated effects at 7 years - Cohort 1

	Hg/Se ratio			Hg
	Q1	Q2-Q3	Q4	All <sup>a</sup>
Finger Tapping preferred hand	-	↑	↓	↓
CPT avg. reaction time (ms)	-	-	↓	↓*
Bender errors	↓	-	-	↓
BNT total correct after cues	↓	↓	↓	↓*
CVLT long delay	-	-	↑	↓

Improvement

↑ 0.10 &lt; p &lt; 0.30

↑↑ 0.05 ≤ p ≤ 0.10

Deficit

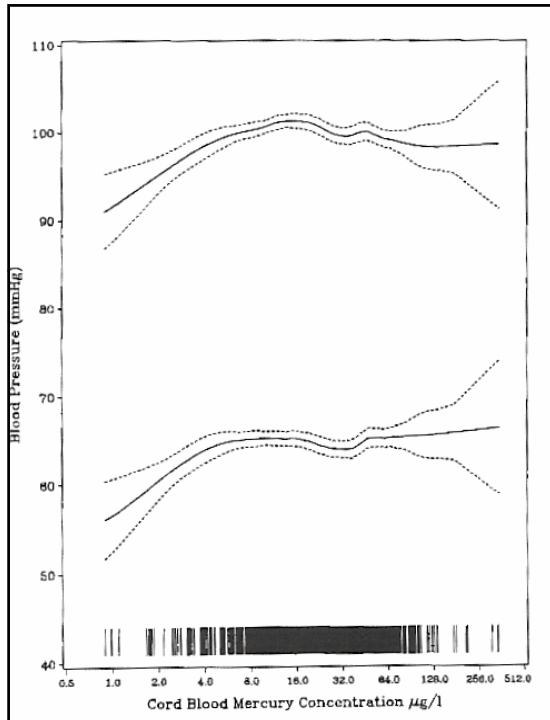
↓ 0.10 &lt; p &lt; 0.30

↓↓ 0.05 ≤ p ≤ 0.10

<sup>a</sup>Grandjean et al. 1997  
Neurotoxicol and Teratol  
19:417-428.

## Conclusion

- On the average, Se was present in cord blood in a molar excess of about 10-fold above Hg
- Se concentrations suggested all children were Se sufficient
- No evidence that Se was a significant protective factor against MeHg neurotoxicity
- Selenium intake can therefore not explain the significant benefits associated with fish intake
- Preventive methods are needed to address MeHg exposures, rather than Se intakes, while maintaining a high fish/seafood intake



Blood pressure at 7 years:

The increase appears at cord blood mercury concentrations below 10 µg/l

Sørensen et al., 1999

## Cardiovascular Function

- Mercury from fish and seafood *may* promote or predispose to the development of heart disease in some studies
- Elevated hair and toenail mercury concentration was associated with
  - Increased risk of coronary heart disease (Salonen et al., 1995)
  - Accelerated progression of carotid atherosclerosis (Salonen et al., 2000)
  - Higher risk of myocardial infarction (Guallar et al. 2002, Yoshizawa et al. 2002)

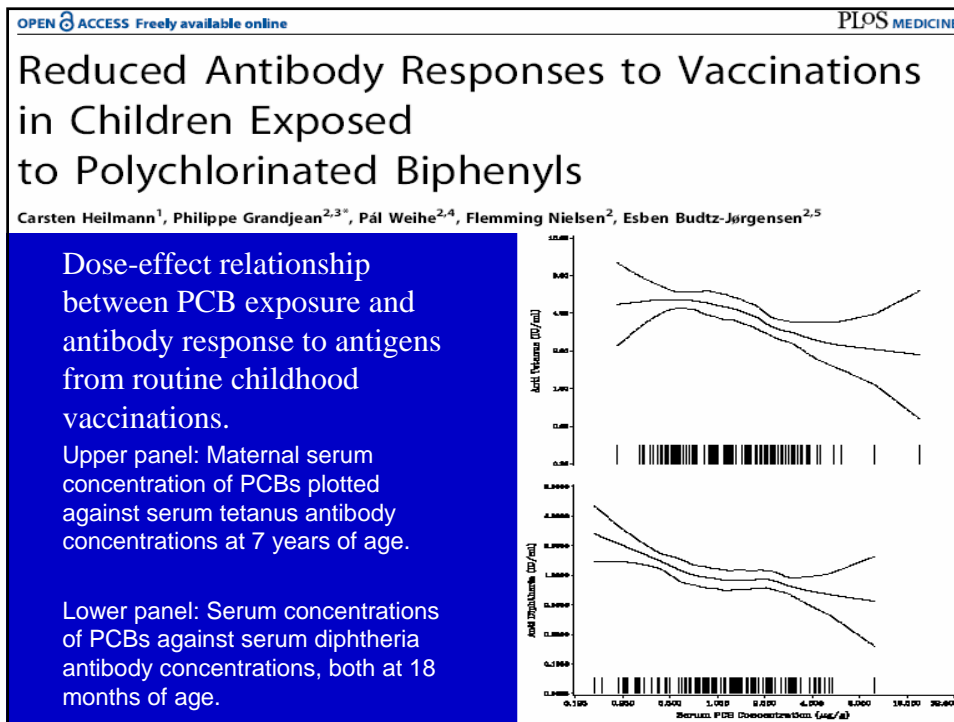
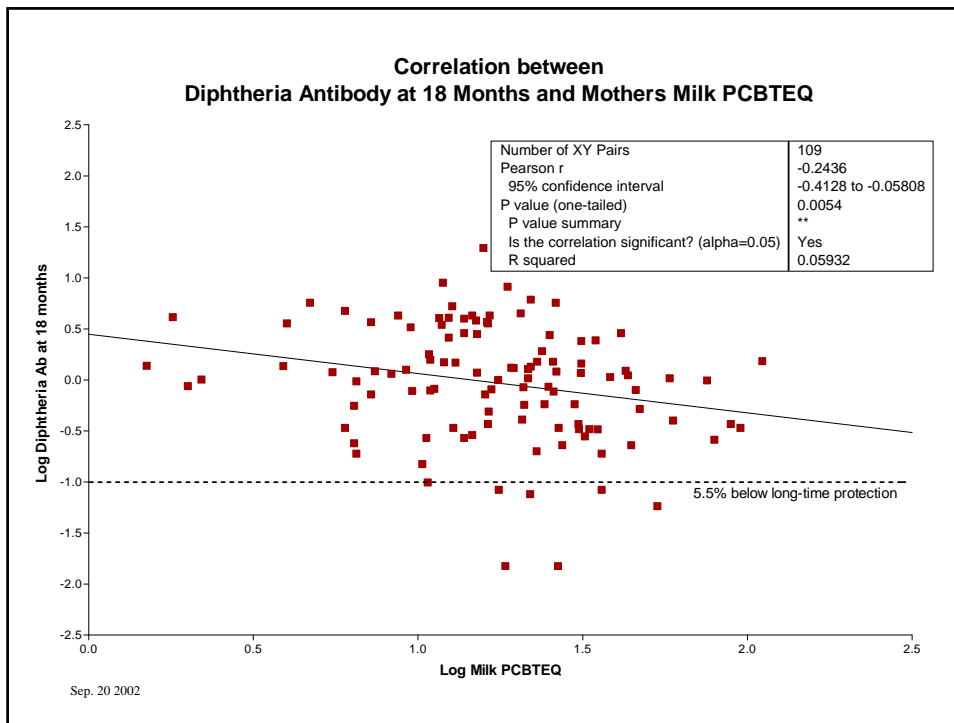
### Change in blood pressure associated with a doubling in mercury exposure

With fish adjustment

Blood Pressure (mmHg)	Exposure Indicators		
	Blood Hg	Nail Hg	Hair Hg (7 yrs ago)
Systolic	5.71 (0.78, 10.6)**	3.81 (-1.73, 9.35)	5.15 (-3.17, 13.5)
Diastolic	2.91 (0.28, 5.55)**	2.92 (0.07, 5.76)**	1.89 (-2.58, 6.36)

### PCB effects in Faroese birth cohort studies

- At age 7 years, the cord PCB concentration was associated with deficits on the Boston Naming Test, the Continuous Performance Test reaction time, and, possibly, on long-term recall on the California Verbal Learning Test
- Increased frequency of otitis med. in Faroese children exposed to high levels of organochlorines. (unpublished)



Do PCBs cause a general reduction in  
immunity  
or do they cause early immune  
dysregulation caused by an adverse  
influence on the thymic function?

## Association between PD and **lifetime** exposure to traditional food



Period	Cases	Controls	Adjusted OR <sup>b</sup> (95% CI)		
	n high/low exposure	n high/low exposure	All	Women	Men
<b>Average in childhood</b>					
Whale meat	64/8	132/21	1.30 (0.53-3.22)	0.71 (0.17-2.98)	2.61 (0.26-25.91)
Whale blubber	61/11	131/22	0.94 (0.42-2.09)	0.95 (0.20-4.49)	1.22 (0.27-5.56)
<b>Average in adulthood</b>					
Whale meat	66/12	74/79	<b>6.53(3.02-14.14)*</b>	<b>7.04 (1.51-32.88)*</b>	<b>10.57(2.42-46.16)*</b>
Whale blubber	67/11	86/67	<b>5.61(2.46-12.81)*</b>	<b>4.24 (1.06-16.97)*</b>	<b>7.63 (1.67-34.74)*</b>
<b>Average during the last year</b>					
Whale meat	43/36	74/78	1.28 (0.72-2.27)	3.04 (0.90-10.18)	0.71 (0.27-1.85)
Whale blubber	45/34	83/69	1.12 (0.62-2.01)	2.24 (0.67-7.41)	0.55 (0.20-1.50)

<sup>b</sup>adjusted for smoking; \*Statistic significant (p<0.05)

Because of collinearity between blubber and whale meat consumption, it is difficult to separate possible effects of these two parameters

## Association between PD and **current** MeHg and POP exposure

	Adjusted OR* (95% CI)		
	All	Women	Men
$\Sigma$ PCB <sup>c</sup>	1.08 (0.86-1.37)	1.21 (0.72-2.03)	0.98 (0.62-1.55)
<i>p,p</i> -DDE	1.01 (0.83-1.22)	1.06 (0.76-1.49)	0.98 (0.68-1.41)
<i>o,p</i> -DDT	0.93 (0.75-1.14)	1.00 (0.62-1.61)	0.80 (0.51-1.25)
HCB	1.02 (0.77-1.34)	1.09 (0.57-2.08)	0.95 (0.60-1.50)
<b><math>\beta</math>-HCH</b>	<b>1.44 (1.05-1.97)*</b>	<b>2.59 (1.03-6.51)*</b>	1.21 (0.73-2.00)
<b>B-Hg</b>	1.08 (0.87-1.34)	<b>1.96 (1.10-3.48)*</b>	0.79 (0.54-1.16)
H-Hg	1.01 (0.83-1.23)	1.47 (0.85-2.55)	0.74 (0.50-1.11)

<sup>a</sup>Adjusted for smoking; <sup>b</sup>2.0 x PCB (138+153+180); <sup>c</sup>(PCB105 + PCB118 + 5\*PCB156) \*10; \*Statistical significant (p<0.05)

## Conclusion



- No significant association between PD and estimated **prenatal** MeHg exposure was found
- Questionnaire information suggested a positive association between PD and **lifetime** consumption of traditional food  $\Rightarrow$  positive association between PD and lifetime POP and MeHg exposure
- **Current** blood concentration levels were fairly similar. However,  $\beta$  - HCH and blood mercury were significantly higher in female PD cases



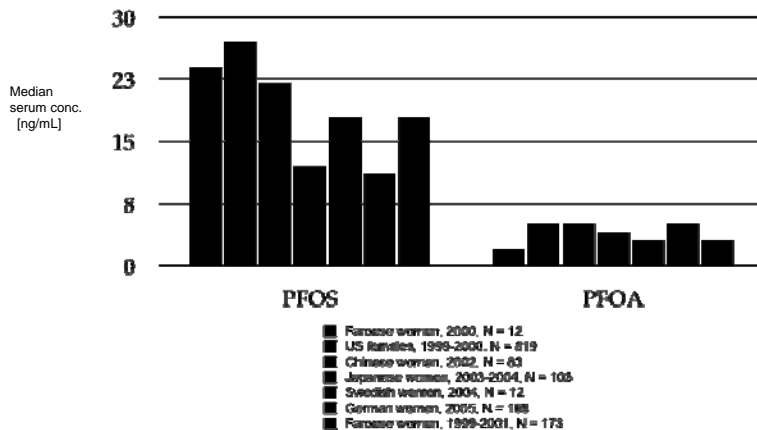
## Endocrine disruptors

Environmental pollutants with hormonal activity especially during development can cause a growing number of health problems later in life

- Polychlorinated biphenyls (PCBs)
- DDT and its main metabolite DDE,
- Phthalates
- Fluorinated chemicals (PFOA/S)
- Bisphenol A



## PFC's in women from selected populations



## Conclusion

- Whale meat is the dominating mercury source in the Faroese population
- Marine fish, commonly consumed in the Faroes, are low in mercury
- Dietary advisories and public information have focused on whale meat and blubber
- Fish consumption recommended

## Clinical conference, Tórshavn clinic



## CHEF: Child Health and the Environment in the Faroes



Website: [www.chef-project.dk](http://www.chef-project.dk)  
Email: [pal@health.fo](mailto:pal@health.fo)



## Environmental contaminants in Pilot whale from NE Atlantic

**Maria Dam**



## Traditional Faroese food



## Environmental monitoring of Pilot whale

- Samples from 50 whales per year; 25 samples from two schools
- Samples are taken of blubber and muscle
- In some ind. also liver and kidney
- Even blood, brain, teeth..



Túrhavn, h. 12. november 1977

### History

AVARING

I seinastuni eru á Heilsumfróðsligu starvsstovuni gjórdar kanningar av kyksilvurinnthaldinum í grind.

Kyksilvurinnthaldið í grindalivur vísir seg at vera so stórt, at tað er sera battiligt at eta hana, og verða fólk tí varað við yvirhóvur at eta grindalivur.

Hóast enn ongar kanningar eru gjórdar av grindanýrum, er nógv, sum ber at tí borði, at eini í nýrum er so nógv kyksilvur, at heldur ikki tey eru nýtandi til fólkamat.

Í grindatvæði er kyksilvurinnthaldið nógv, nógv minni enn í livur. Tó er tað so stórt, at vit fyrstila vilja mæla fólk frá at eta grind meira enn einu ferð um vikuna.

Lagt skal verða afturat, at eingin vandi frá kyksilvuri er í spiki. Kanningarar heida á, og útslitini skulu verða kannað so við og við.

Landsdýralæknin og landslæknin

Sample	PCB and Arochlor 1254-1260, ng/g lw	Sample	PCB and Arochlor 1254-1260, ng/g lw
2 young 2 adults blubber 4 Faroe Islands 1974 Pilot whale	~38	older 14 fem 24 mal abdominal fat 38 Faroe Islands 1975-76 People	~38
adults blubber 124 Faroe Islands 1987 Pilot whale	~124	young 44 fem 15 mal blubber 55 Faroe Islands 1987 Pilot whale	~55

Humane data: Kraul, I. et al. 1977. Persistente organiske klorerede forbindelser og kviksølv i et humant materiale indsamlet på Færøerne i 1975-1976. Kgl. Veterinær og Landbohøjskole, Afd Farm.. og tox.. Kbh.

## “Ranking list” of contaminants in Pilot whales

Pilot whale young  
units ng/g fat or ng/g meat

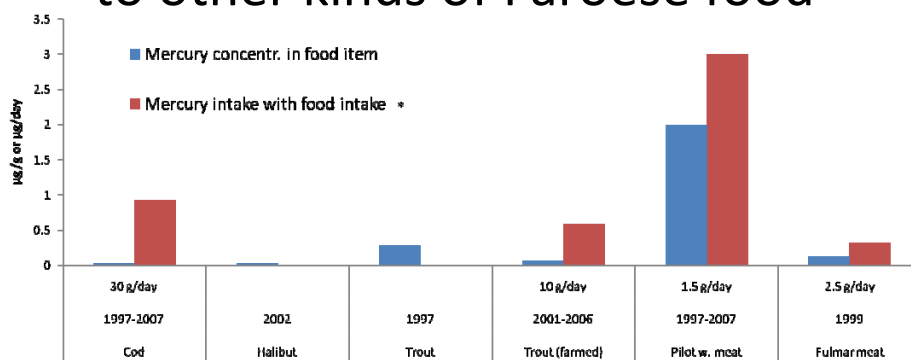
- PCB, DDT : 10 000
- Toxaphene: 8 000
- Chlordanes: 4 000
- Mercury: 1 000
- PBDE group: 1 000
- PFOS group: 500 ng/g liver



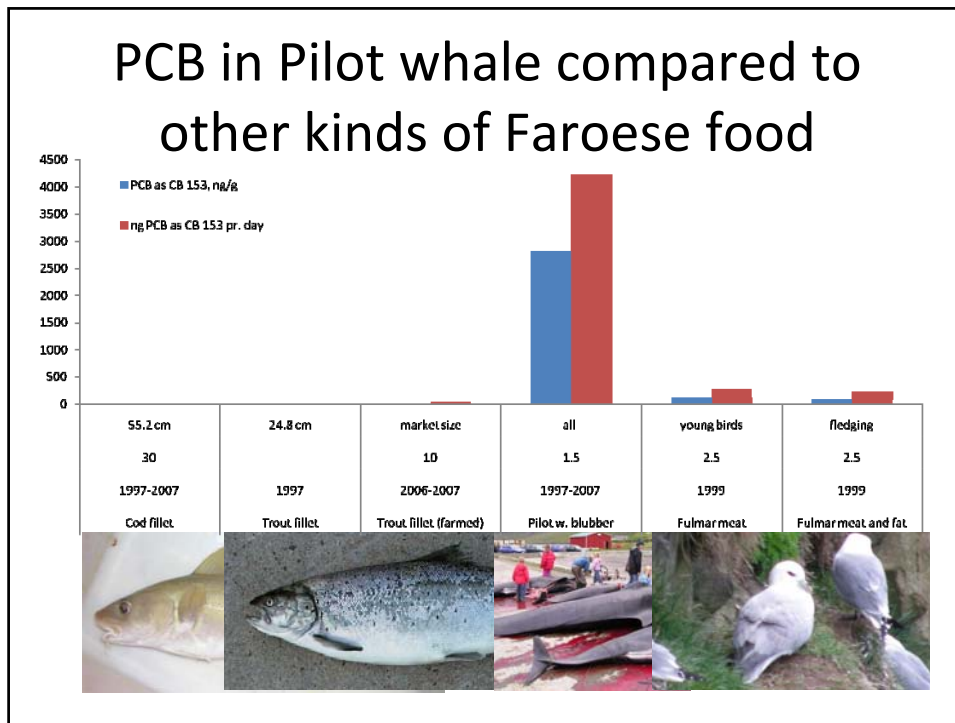
Red compounds are incl. in the Stockholm POP Convention.

Large parts of the orange compounds were added to the Convention in 2009.

## Mercury in Pilot whale compared to other kinds of Faroese food



\*Info on diet from: A.S. veyne "Færøske kvinners kostvaner i graviditetens tredje trimester" [Dietary habits of Faroese women during third trimester of their pregnancy]. Master of Public Health thesis, MHP 2006:10, Nordiska hogskolen for folkhalsvetenskap, Gothenburg, Sweden, www.nhv.se

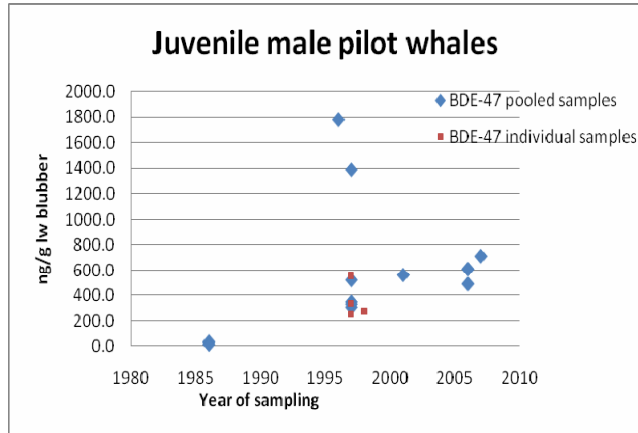


### Concentration of PBDE in Faroese food:

ng/g lipid	Halibut	Cod	Sheep / lamb	Cows butter	Cows milk	Fulmar	Pilot whale	Pilot whale	Mothers milk*
Matrix	muscle	muscle	suet	butter	whole milk	subcut fat	liver	blubber	milk
n (# analyses)	16 (4)	16 (4)	30 (4)	2	2	10	15	171	9
Sampling year	2005	2005	2005	2005	2005	2005	2004	1994-98	1998-99
Fat %	2%	0%	90%	91%	3%	92%	2%	66%	3%
BDE 47	3.0	7.0	0.0	0.1	0.0	4.7	15.4	569	1.9
BDE 100	0.4	1.3	0.0	0.0	nd	0.7	5.3		1
BDE 99	0.5	1.1	0.0	0.1	0.1	1.0	9.4	114	0.84
BDE 154	0.4	0.4	0.0	nd	nd	1.1	30.1	32	
BDE 153	nd	nd	0.0	0.0	nd	0.3	9.7	10	2.4
sum PBDE									
LB	5.5	11.9	0.2	0.3	0.1	8.4	88.6	840	7.2

nd:<LOD 0.01, \* Fangstrom et al., 2005

## PBDE in Pilot whales

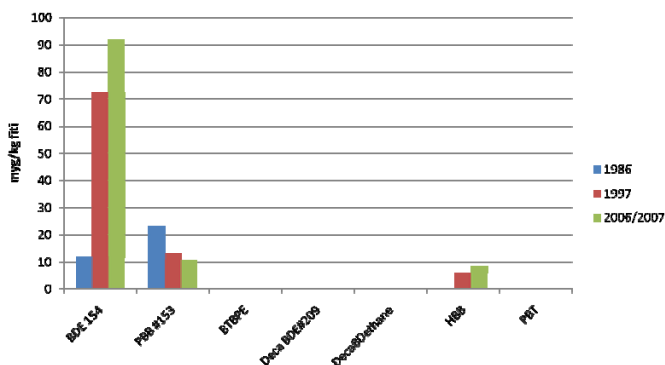


Data mainly from:

**"New" POPs in marine mammals in Nordic Arctic areas during three decades.**

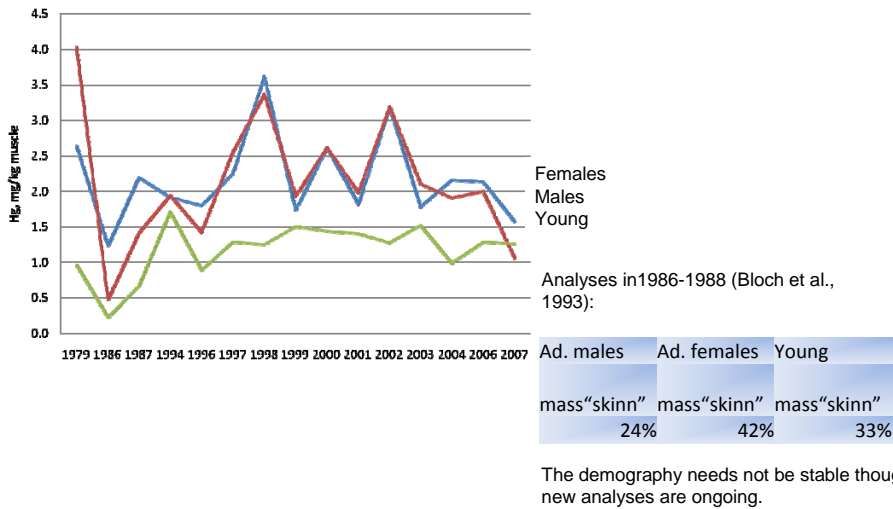
- a study supported by the Nordic Council of Ministers aiming at depicting possible trends in "new" contaminants in marine mammals in Nordic Arctic waters over three decades.

### Other brominated flame retardants in Pilot w. blubber

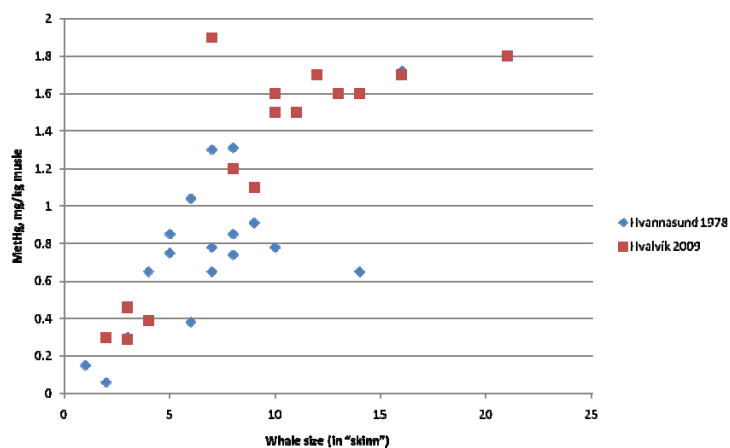


Abbreviation	CAS nr.	Name
BTBPE	37853-59-1	1,2-bis(2,4,6-tribromophenoxy)-ethane
TBECH	3322-93-8	tetrabromoethylcyclohexane/1,2-Dibromo-4-(1,2-dibromoethyl)cyclohexane
HBB	87-82-1	hexabromobenzene
PBT	87-83-2	pentabromotoluene
DecaBDEthane	84852-53-9	1,2-bis(pentabromophenyl) ethane / 1,1'-(Ethane-1,2-diyl)bis(pentabromobenzene)
PBB-153	59080-40-9	/ Firemaster 2100 an Saytex 8010 2,2',4,4',5,5'-hexabromobiphenyl

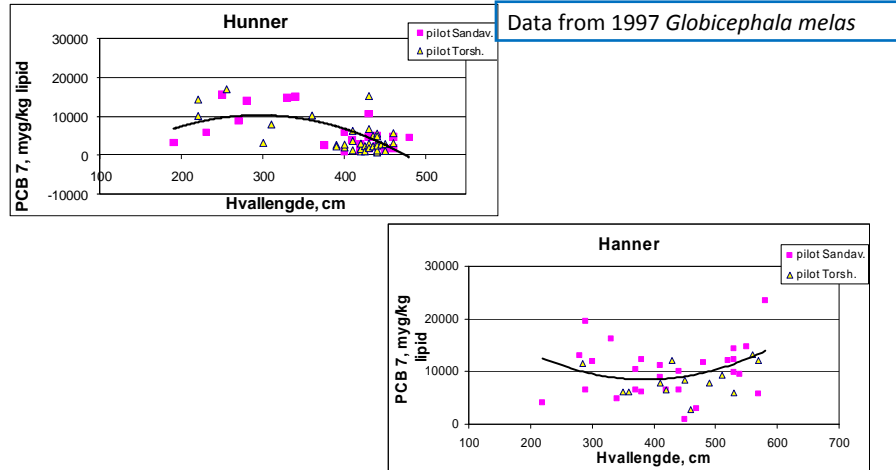
## Mercury in Pilot whale muscle



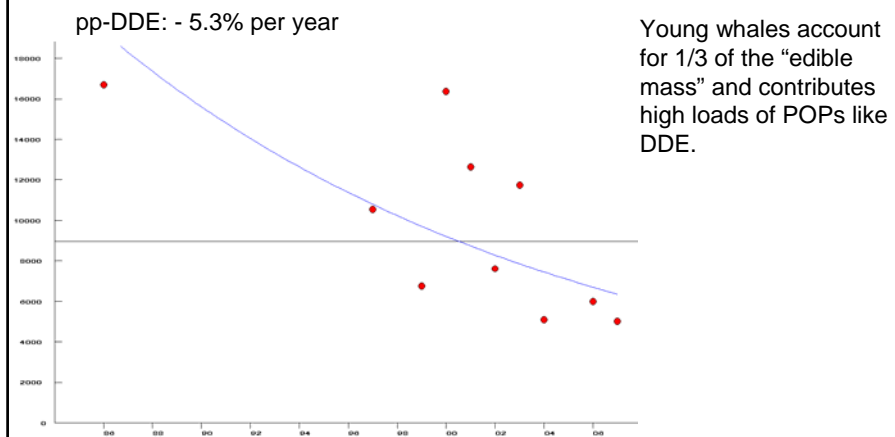
## Analyses in 2010: Met-Hg is approx 100% of tot Hg



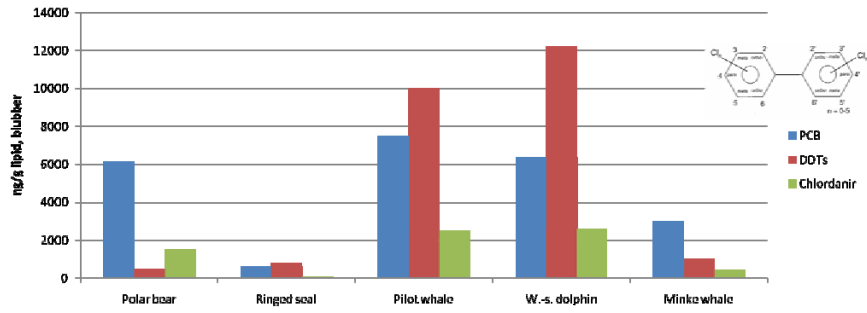
PCB; an overall pattern with decreasing conc. with age in females and increasing in males;



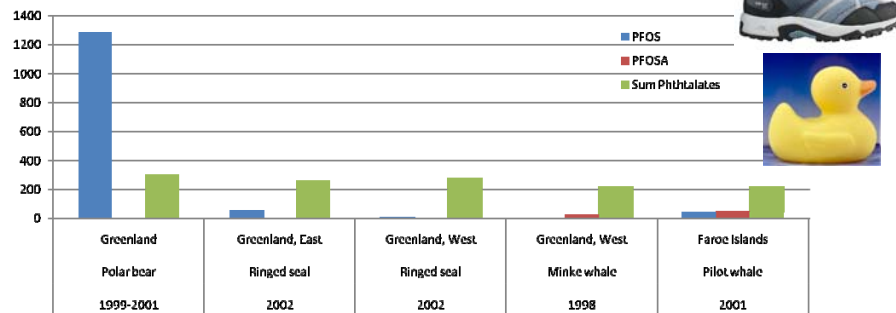
DDT- is similar to PCB but decreases significantly



## Then what about other marine mammals?



## Then what about other marine mammals?



## Then what do we know about nutritional value of pilot whale?

Whale meat	Energy	Protein	FAT			Carbohydrate	Cholesterol	Water	Authority
			Total	Saturated	Poly unsaturated				
per 100 g net	KJ	g	g	g	g	g	mg	g	
Blubber, fresh, uncooked	2582	3	65.7	10.3	9.34	0	31.3	1.9	
Whale meat, fresh, uncooked, winter catch	545	24.6	3.3	0.9	0.5	0.18	71.1	1.6	
Whale meat, fresh, uncooked, summer catch	462	24.6	0.74			0.62	73.0	1	
Whale meat, fresh, soaked, winter catch	625	19.7	7.5			0.32	65.5	1	

Whale meat	VITAMIN						MINERALS					Authority	
	A RE	D µg	B1 mg	B2 mg	Niacin NE	C mg	Sodium mg	Potassium mg	Calcium mg	Iron mg	Zinc mg		Selenium µg
Blubber, fresh, uncooked	1200	0.03	0.04		0	25	1220	15.3	43.1	7.5	185	1.6	6.9
Whale meat, fresh, uncooked, winter catch	100	0.18	0.2		0	390	1809	11.5	63.3	6.4	161	1	
Whale meat, fresh, uncooked, summer catch					0	4330	220	130	46.9	5.4	161	1	
Whale meat, fresh, soaked, winter catch					0								

Poulsen, M. 1995. Faroese Food Composition Tables, FE&V Agency Faroe Islands. Available at [www.hfs.fo](http://www.hfs.fo)

## Selenium is well known though

Table 3.7 Heavy metals in pilot whale muscle. Number and size of the analysed whales is given in Table 2.3

Year	Date	Age and sex group	Juveniles				Adult females				Adult males			
			Dry weight %	Hg	Cd	Se	Dry weight %	Hg	Cd	Se	Dry weight %	Hg	Cd	Se
2001	06.07.01	Min	24	0.29	0.008	0.500	24	1.52	0.090	0.52	26	1.8	0.108	0.476
		Max	29	2.08	0.208	0.936	33	2.3	0.775	1.22	28	2.9	0.206	0.494
		Mean	<b>26.5</b>	<b>1.17</b>	<b>0.11</b>	<b>0.64</b>	<b>27.5</b>	<b>1.90</b>	<b>0.36</b>	<b>0.64</b>	<b>27.0</b>	<b>2.43</b>	<b>0.17</b>	<b>0.49</b>
		Std. dev.	1.60	0.70	0.06	0.15	2.47	0.27	0.18	0.18	1.00	0.57	0.05	0.01
2002	03.09.02	Min	24	0.31	0.006	0.546	24	1.51	0.147	0.468	25	2.48	0.144	0.475
		Max	28	2.02	0.133	0.884	29	6.92	1.02	1.512	30	3.71	0.259	0.945
		Mean	<b>26.1</b>	<b>1.32</b>	<b>0.069</b>	<b>0.653</b>	<b>26.6</b>	<b>3.15</b>	<b>0.44</b>	<b>0.89</b>	<b>27.3</b>	<b>3.18</b>	<b>0.203</b>	<b>0.669</b>
		Std. dev.	1.21	0.72	0.043	0.124	1.36	1.59	0.25	0.37	1.80	0.37	0.039	0.168
2003	03.08.03	Min	25	0.22	0.04	0.6	20	1.15	0.04	0.44	26	1.5	0.04	0.53
		Max	37	2.28	0.07	1.5	32	3.57	0.25	0.92	31	3.03	0.09	0.71
		Mean	<b>29.45</b>	<b>1.52</b>	<b>0.05</b>	<b>0.85</b>	<b>26.90</b>	<b>1.78</b>	<b>0.1</b>	<b>0.66</b>	<b>28.75</b>	<b>2.11</b>	<b>0.06</b>	<b>0.61</b>
		Std. dev.	3.83	0.51	0.01	0.27	3.54	0.69	0.07	0.16	2.06	0.67	0.02	0.08
2004	08.06.04	Min	24	0.46	0.01	0.42	26	1.28	0.09	0.42	26	1.24	0.03	0.42
		Max	29	1.52	0.07	0.73	36	4.44	0.43	2.4	31	2.54	0.36	0.58
		Mean	<b>27.7</b>	<b>0.99</b>	<b>0.04</b>	<b>0.58</b>	<b>29.3</b>	<b>2.16</b>	<b>0.22</b>	<b>0.77</b>	<b>27.9</b>	<b>1.90</b>	<b>0.17</b>	<b>0.51</b>
		Std. dev.	1.86	0.54	0.02	0.12	2.57	0.92	0.11	0.53	1.68	0.44	0.12	0.06
2006	28.08.06	Min	27	0.36	0.008	0.59	-	1.77	0.17	-	-	1.75	0.12	-
		Max	32	2.29	0.196	1.7	-	4.46	0.86	-	-	2.16	0.27	-
		Mean	<b>28.7</b>	<b>1.16</b>	<b>0.08</b>	<b>0.80</b>	-	<b>2.32</b>	<b>0.38</b>	-	-	<b>2.04</b>	<b>0.18</b>	-
		Std. dev.	1.5	0.51	0.05	0.31	-	0.64	0.23	-	-	0.19	0.08	-
2006	06.09.06	Min	27	0.66	0.02	0.49	-	0.29	-	-	-	-	-	-
		Max	34	2.25	0.10	0.71	-	3.0	-	-	-	-	-	-
		Mean	<b>30.6</b>	<b>1.40</b>	<b>0.06</b>	<b>0.60</b>	-	<b>1.95</b>	<b>0.15</b>	-	-	<b>1.95</b>	<b>0.15</b>	-
		Std. dev.	2.8	0.8	0.02	0.1	-	0.4	0.05	-	-	0.4	0.02	-

Hoydal and Dam, 2009. AMAP...2005-2008. [www.us.fo](http://www.us.fo)

Reports are available at: [www.us.fo](http://www.us.fo)

Data are available at [www.us.fo](http://www.us.fo) (search for ENVOFAR)





UNIVERSITY OF ICELAND  
SCHOOL OF HEALTH SCIENCES  
FACULTY OF MEDICINE  
Department of Physiology



# n-3 Long-chain PUFA in health and disease

Guðrún V. Skúladóttir

Workshop in Copenhagen January 14, 2011

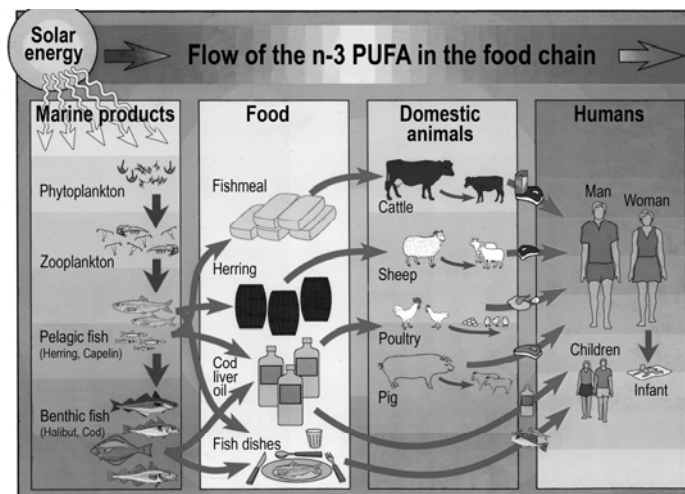
## Introduction

- Historical background
  - Marine n-3 LC-PUFA consumption of Icelandic population and n-3 LC-PUFA status in their body
- Human studies
  - Pregnancy and birth outcome related to n-3 LC-PUFA consumption
  - Open heart surgery and risk of atrial fibrillation related to n-3 LC-PUFA consumption
  - Intake of fish and fish oil in adolescence and midlife and risk of coronary heart disease in older women

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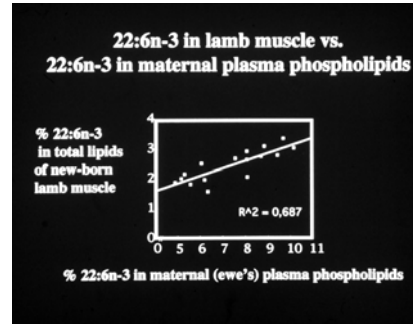
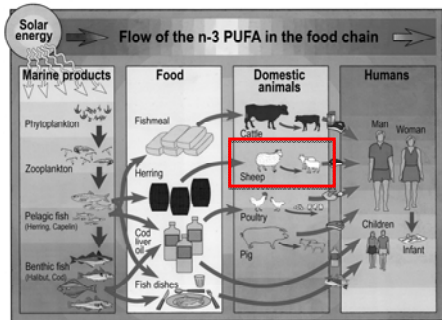
Iceland has been a community with traditional fish and cod liver oil consumption



Relatively high levels of circulating n-3 LC-PUFA in Icelanders compared to other populations

The International Handbook of Behavior, Diet and Nutrition. Dietary n-3 polyunsaturated fatty acids and brain lipid fatty acid composition. GV Skuladottir. In press. Workshop in Copenhagen January 14, 2011

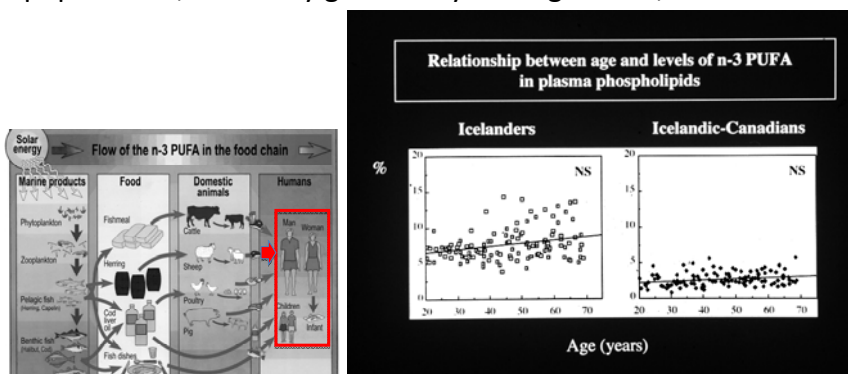
In Iceland it has been a customary to supplement ewes diet with fish meal, herring or fish oil in December during breeding season and prior to the lambing season in the spring



Ewes where fed 80 g fish meal per day during gestation.  
GV Skúladóttir et al. Unpublished data

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- In the late eighties crude mortality for ischemic heart diseases was higher among Manitoban residents of pure Icelandic descent than among the Icelandic population
- In 1990 the fatty acid levels in plasma phospholipids of these two populations, unusually genetically homogeneous, were studied



GV Skúladóttir et al. Lipids 1995;30:649-655.

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## Conclusion

(GV Skúladóttir *et al.* Lipids 1995;30:649-655)

The results from this study supported the ideas that n-3 LC-PUFA, such as Icelanders obtain through their consumption of fish, fish oil, and Icelandic lamb, can afford protection from atherosclerotic disease, even in the face of a diet that in other respects may be counted as atherogenic

- (fat contributed 41% of total dietary energy, with the contribution of saturated fat amounting to 20%)

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## Iceland

- A community with traditional fish and cod liver oil consumption
- Average birthweight is among the highest worldwide
  - Opportunity to study the contribution of cod liver oil (i.e. n-3 LC-PUFA) consumption to important health aspects for mother and newborn infant

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## Subjects

Observational study on healthy and low-risk Icelandic pregnant women, who attended a routine first visit 1999-2001.

Pregnant women attended between 11 and 15 weeks and between 34 and 37 weeks of gestation

- Food frequency questionnaire for the previous three months

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**Table 1 Maternal daily intake of fish and number of pregnant women consuming liquid cod liver oil. Values are expressed as mean [SD] or n (%).**

	Week of pregnancy	
	11 <sup>th</sup> to 15 <sup>th</sup>	34 <sup>th</sup> to 37 <sup>th</sup>
	n = 436	n = 358
Fish ( g/day)	29 [28]	27 [20]
<b>Liquid cod liver oil</b>	<b>63 (14.5)</b>	<b>62 (17.4)</b>
Concentrated cod liver oil capsules	134 (30.7)	123 (34.4)

**Liquid cod liver intake in first trimester was positively correlated with birth weight after adjustment for gestational age at birth and other confounding factors.**

**Olafsdottir AS et al. BJOG 2005**

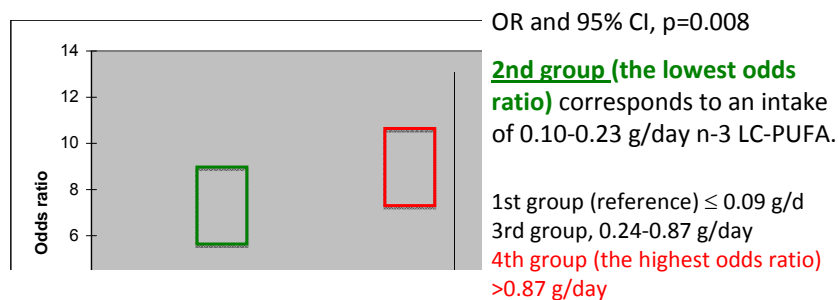
**Table 3: Linear regression model for birth weight (n = 350)**

	Regression Coefficient	P	95% Confidence Interval	
			lower bound	upper bound
(Constant)	-3408.7	<0.001	-5173.1	-1644.4
<b>Cod liver oil in first trimester (yes/no)</b>	<b>132.1</b>	<b>0.023</b>	18.3	246.0

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**Result suggests a u-shaped curve for the odds of hypertensive disorders in pregnancy.**

**Olafsdottir et al. BJOG. 2006;113:301-309.**



**Figure 1: Odds ratios and 95% CI for hypertensive disorders in pregnancy by centiles of n-3 LCPL in early pregnancy. Groups were divided into 1) 10th centile (reference), 2) 11-50th centile, 3) 51-90th centile and 4) above 90th centile. Weight gain**

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## Conclusion

### Benefits

For healthy Icelandic women without pregnancy complications, regular intake of liquid cod liver oil early in pregnancy is to be considered as positive for the infants health.

Olafsdottir AS *et al.* BJOG 2005;112;424-429.

### Risk

High doses of n-3 LC-PUFA in early pregnancy, or other nutrients found in liquid cod liver oil, may increase the risk of developing hypertensive disorders in pregnancy.

Olafsdottir AS *et al.* BJOG 2006;113;301-309.

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  - Marine n-3 LC-PUFA consumption of Icelandic pregnant women and birth weight
  - n-3 LC-PUFA blood status of Icelandic patients undergoing open heart surgery and risk of atrial fibrillation
  - Intake of fish and fish oil in adolescence and midlife and risk of coronary heart disease in older women

## Atrial fibrillation - AF

- The most common cardiac arrhythmia
- Frequently occurs as a complication of cardiac surgery (postoperative AF=**POAF**)
- Evidence linking POAF with **inflammation**
- It has been postulated that the **anti-arrhythmic and anti-inflammatory effects of n-3 LC-PUFA** may decrease the risk of POAF following open heart surgery

n-3 LC-PUFA treatment has **beneficial effects** for the prevention of atrial fibrillation after coronary artery bypass (CABG) surgery

- Calo *et al.* J Am Coll Cardiol 2005;45:1723–1728.

An Italian study showed that the incidence of POAF in patients **supplemented with capsules containing EPA and DHA as ethyl esters** for at least 5 days before surgery was 15% compared with 33% in the control group

- Heidt *et al.* Thorac Cardiovasc Surg 2009;57:276–8

A German study showed that the incidence of POAF in patients who received **an intravenous infusion of EPA and DHA as emulsion of highly refined fish oil, at least 12 hours** preoperatively and immediately following surgery was 17.3% compared with 30.6%, in the control group

- **Not blinded placebo-controlled studies**

Two studies found **no benefit** of short-term fish oil supplementation on the risk of AF following coronary artery bypass graft (CABG) surgery

- A British study performed by Saravanan *et al.* *Circ Arrhythm Electrophysiol* 2010;3:46-53.
- An Icelandic study performed by Heidarsdottir *et al.* *Europace* 2010;12:356–363.
  - 170 patients undergoing open heart surgery were recruited between August 2007 until middle of May 2009
- **Both studies were blinded placebo-controlled studies**

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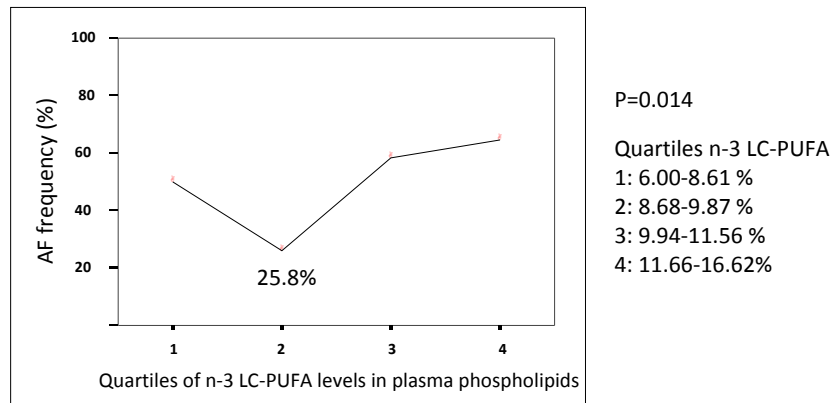
## Baseline levels (%) of EPA and DHA in plasma phospholipids

	EPA	DHA
Italy (n=61)	0.81 (0.71, 0.92)	3.77 (3.53, 4.03)
Germany (n=203)	1.05 (0.98, 1.12)	3.79 (3.65, 3.93)
UK (n=178)	1.03 (0.95, 1.12)	4.03 (3.85, 4.21)
Iceland (n=158)	2.21 (0.84, 9.15)	6.06 (3.47, 10.63)

Values are median; 95% CI in parantheses

The results from our Icelandic study suggests a u-shaped curve for the relationship between the incidence of AF and quartiles of total n-3 LC-PUFA levels in plasma phospholipids.

Gudrun V. Skuladottir et al., Eur J Clin Invest (in press)



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## Conclusion

- **Benefit**
  - n-3 LC-PUFA administration may be beneficial for prevention of POAF in patients with very low baseline levels of these fatty acids in blood.
- **Risk**
  - relatively high levels of n-3 LC-PUFA may increase the risk of POAF.

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n-3 Long-chain PUFA in  
health and disease

“Moderation in all things”

Aristotles

Arja Erkkilä

## Fish intake and inflammatory markers - gene expression and lipidomics data



### A University with Three Campuses

- The University of Eastern Finland has three campuses in Joensuu, Kuopio and Savonlinna.
- Common operating principles on all campuses.
- Each of the campuses has a distinct profile.
- Cooperation between the campuses is active.

[www.uef.fi](http://www.uef.fi)



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## Background

- Sea mammals are not consumed in Finland
- Marine fatty acids and fish are of high interest

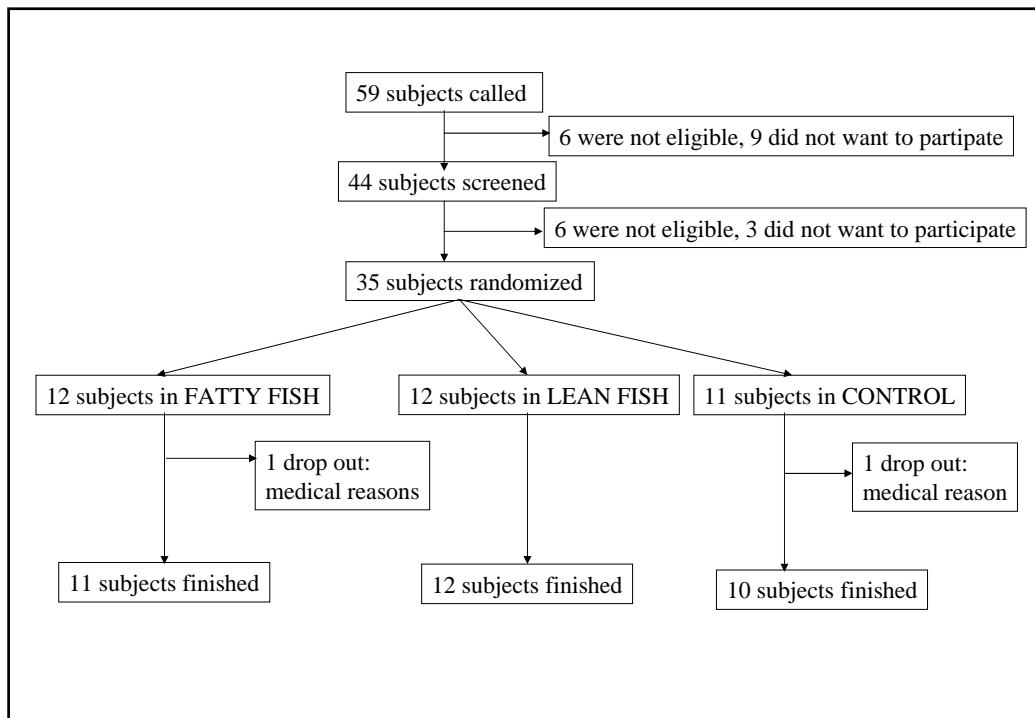
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## Aim

- To examine the effects of lean and fatty fish intake on cardiovascular risk factors in patients with coronary heart disease
- Inclusion criteria:
  - MI or unstable ischemic attack
  - Use of betablockers
  - Age under 70 years
  - Normal sinus rhythm
  - TG  $\leq$  3,5 mmol/l, s-cholesterol  $\leq$  8 mmol/l
  - BMI 18,5-30 kg/m<sup>2</sup>
  - P-glucose  $\leq$  7,0 mmol/l

## Intervention diets, duration 8 weeks

- Fatty fish
  - At least 4 meals per week
  - Choose from salmon, rainbow trout, Baltic herring, vendace or tuna
- Lean fish
  - At least 4 meals per week
  - Choose from pike, pike-perch, perch, saithe or cod
- Control diet
  - Maximum 1 fish meal per week
- All the participants were advised to eat a healthy, cholesterol lowering diet



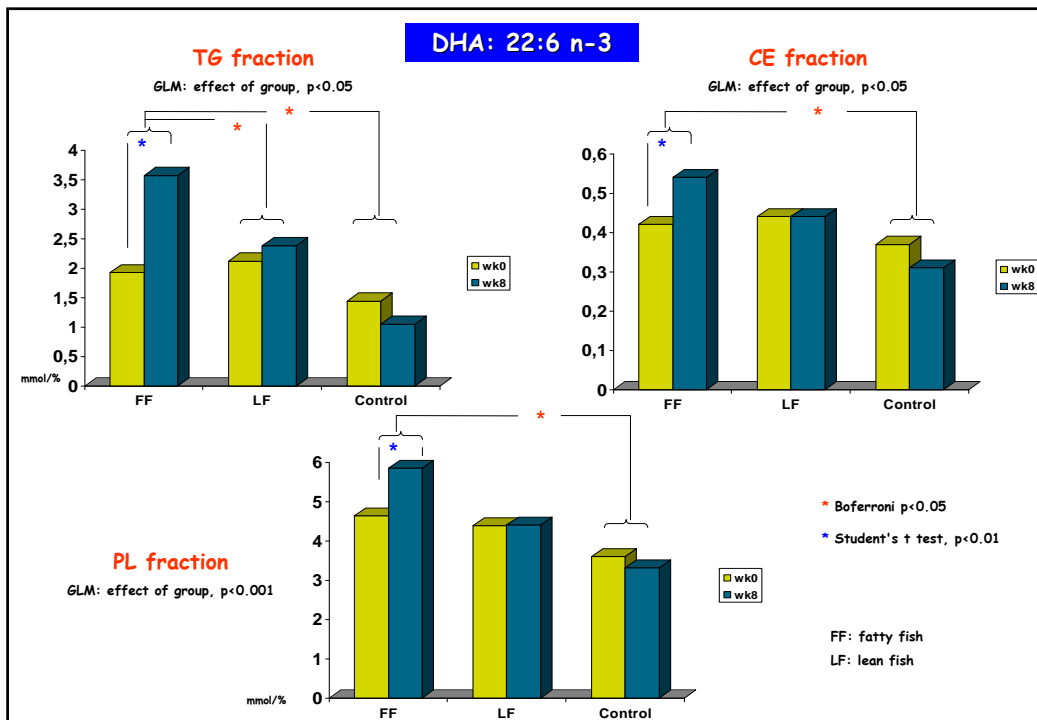
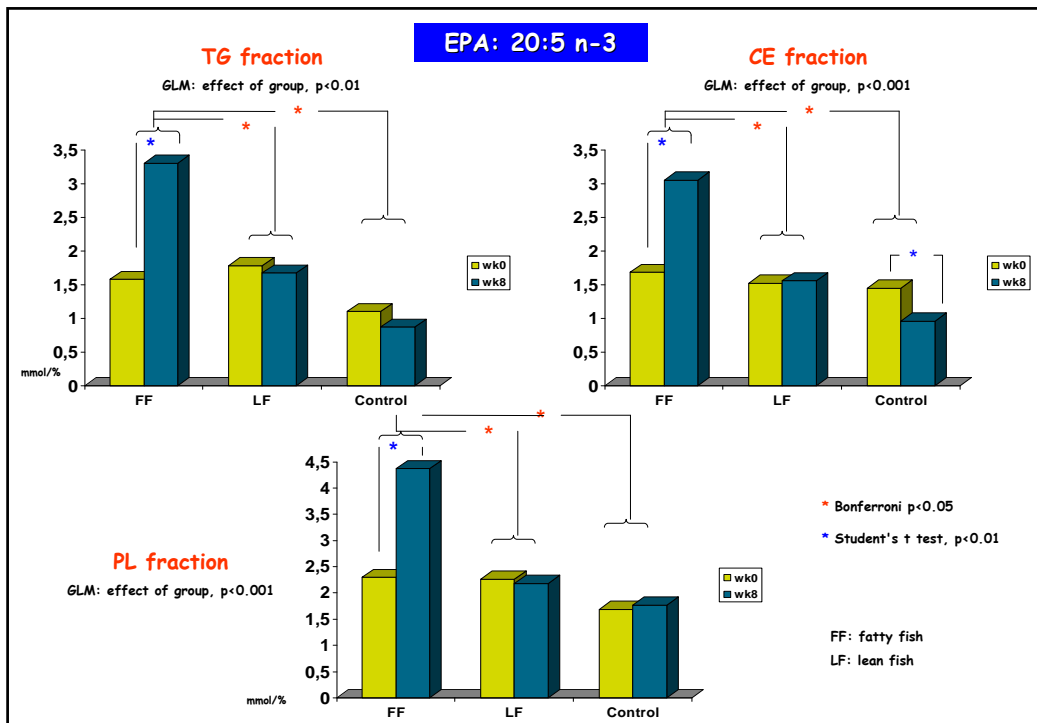
## Characteristics of the participants

Variable	Fatty fish (n=11)	Lean fish (n=12)	Control (n=10)	p- value
Sex, men/women, n	8/3	10/2	9/1	0.58
Age, y	62.1±6.3	60.7±5.1	60.2±6.4	0.75
Myocardial infarction, n	5	10	5	0.06
Coronary bypass surgery, n	2	4	0	0.15
Balloon angiography, n	8	9	9	0.58
<i>Medications, n</i>				
Lipid lowering drug	11	12	10	
Beta blocker	11	12	10	
Aspirin	10	11	8	0.66
ACE inhibitor	3	6	6	0.30
Ca antagonist	3	4	2	0.78
Anticoagulant	4	4	5	0.71
Nitrate	2	4	3	0.70

## Dietary compliance

Intake	Fatty fish (n=11)	Lean fish (n=12)	Control (n=10)
Fish meals/wk	4.3±0.4	4.7±1.1	0.6±0.4
EPA+DHA, g/d	1.07±0.41	0.44±0.14	0.16±0.11

Mean±SD



## Blood pressure

Variable	Fatty fish (n=11)	Lean fish (n=12)	Control (n=10)	p for intervention *group
Systolic pressure, mm Hg				0.01
0 wk	122±11	123±10	126±14	
4 wk	125±11	120±12	122±13	
8 wk	127±9	118±11	125±15	
Diastolic pressure, mm Hg				0.02
0 wk	80±5	82±8	81±8	
4 wk	81±6	80±8	79±6	
8 wk	82±4	78±7	81±8	

Mean±SD, \* p<0.05 within group change, P values are adjusted for sex

## Serum lipids

Variable	Fatty fish (n=11)	Lean fish (n=12)	Control (n=10)	p for intervention *group
Total cholesterol, mmol/l				0.29
0 wk	3.77±0.60	3.75±0.73	4.72±0.80	
4 wk	3.78±0.56	3.74±0.62	4.37±1.03	
8 wk	3.51±0.62	3.71±0.57	4.32±0.77	
LDL cholesterol, mmol/l				0.87
0 wk	1.88±0.34	2.04±0.61	2.58±0.59	
4 wk	1.97±0.42	2.09±0.57	2.59±0.84	
8 wk	1.92±0.28	2.04±0.48	2.47±0.62	

Mean±SD  
P values are adjusted for sex

## Serum lipids

Variable	Fatty fish (n=11)	Lean fish (n=12)	Control (n=10)	p for intervention *group
HDL cholesterol, mmol/l				0.02
0 wk	1.39±0.43	1.29±0.34	1.43±0.48	
4 wk	1.41±0.32	1.14±0.29	1.37±0.51	
8 wk	1.51±0.44	1.27±0.32	1.30±0.37	
Triglycerides, mmol/l				0.25
0 wk	1.26±0.67	1.10±0.64	1.92±1.18	
4 wk	1.27±0.52	1.27±0.72	1.62±0.77	
8 wk	1.09±0.44	1.08±0.59	1.66±0.47	

Mean±SD

P values are adjusted for sex

## Apolipoproteins

Variable	Fatty fish (n=11)	Lean fish (n=12)	Control (n=10)	p for intervention *group
Apo A1, g/l				0.03
0 wk	1.42±0.32	1.30±0.20	1.52±0.26	}*
8 wk	1.43±0.30	1.30±0.19	1.40±0.23	
Apo B, g/l				0.35
0 wk	0.76±0.18	0.76±0.19	1.02±0.23	
8 wk	0.76±0.15	0.76±0.13	0.95±0.19	

Mean±SD, P values are adjusted for sex

\*within group change p<0.05

## Coagulation

Variable	Fatty fish (n=11)	Lean fish (n=12)	Control (n=10 wk)	p (intervention *group)
Fibrinogen, g/l				0.93
0 wk	3.47±0.42	3.67±0.75	4.02±0.72	
8 wk	3.46±0.47	3.62±0.96	4.03±0.69	
D-dimer, mg/l				0.03
0 wk	0.12±0.12	0.49±1.35	0.20±0.25	
8 wk	0.08±0.07	0.38±0.92	0.18±0.19	
PAI-1, AU/ml				0.12
0 wk	16.6±9.45	23.9±18.7	20.0±8.5	
8 wk	19.4±7.5	19.3±14.1	16.7±7.9	

## Inflammatory markers

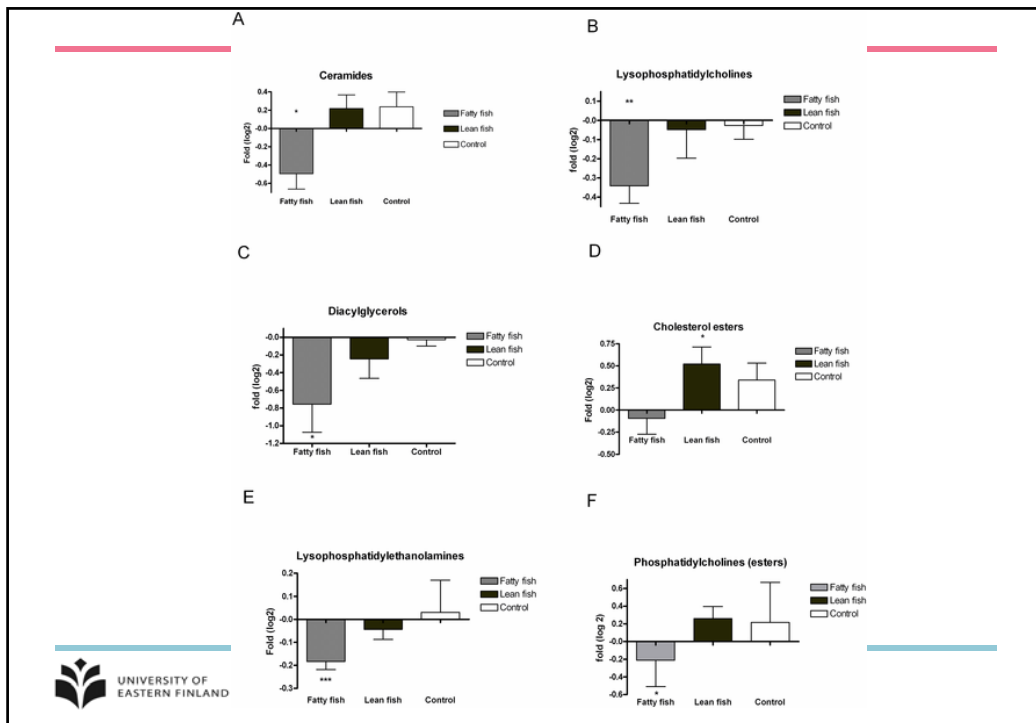
Variable	Fatty fish (n=10)		Lean fish (n=11)		Control (n=6)		p for intervention *group
	0 wk	8 wk	0 wk	8 wk	0 wk	8 wk	
CRP, mg/l	0.58 (0.36-2.13)	0.76 (0.23-1.60)	1.17 (0.50-2.85)	0.80 (0.54-3.22)	1.63 (0.25-4.53)	1.33 (0.50-4.33)	0.69
TNF- $\alpha$ , pg/ml	1.27 (0.83-1.59)	1.17 (0.57-1.82)	1.37 (0.78-1.69)	1.16 (0.79-1.32)	1.28 (1.05-1.47)	1.08 (0.89-1.25)	0.81
IL-1 $\beta$ , pg/ml	0.78±0.08	0.80±0.13	0.83±0.14	0.84±0.16	0.82±0.08	0.79±0.07	0.56
IL-6, pg/ml	1.58 (0.91-3.98)	1.57 (0.82-4.13)	1.40 (0.89-2.12)	1.50 (0.90-1.99)	1.44 (0.94-4.12)	1.47 (1.07-1.47)	0.94

## Inflammatory markers

Variable	Fatty fish (n=10)		Lean fish (n=11)		Control (n=6)		p for intervention *group
	0 wk	8 wk	0 wk	8 wk	0 wk	8 wk	
VCAM-1, ng/ml	618±122	618±132	545±53	555±80	610±80	562±95	0.06
ICAM-1, ng/ml	186±49	189±43	<b>208±32</b>	<b>203±32*</b>	183±69	169±57	0.04
P-selectin, ng/ml	75±24	73±26	81±40	79±43	96±46	91±51	0.39
E-selectin, ng/ml	32±8	33±8	27±12	26±10	41±18	36±13	0.03

## Correlations in fatty fish group (n=10)

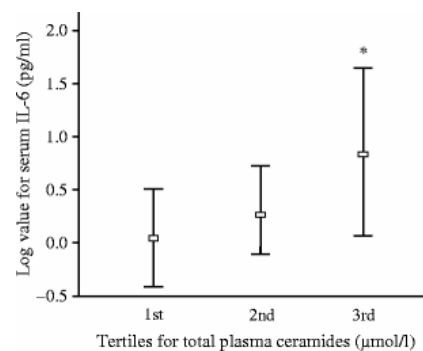
Change in mRNA expression in PBMCs	Change in AA:EPA in CE		Change in AA:EPA in PL	
	r	p	r	p
TNF	0.22	0.53	0.21	0.56
IL1B	<b>0.60</b>	<b>0.06</b>	<b>0.86</b>	<b>0.002</b>
SELP	0.29	0.43	0.32	0.37
ICAM1	0.14	0.70	0.37	0.29



### Correlations among inflammatory markers and ceramides and diacylglycerols at the baseline

	IL-6	TNF- $\alpha$	hsCRP
Ceramides	0.59*	0.24	0.09
Diacylglycerols	0.33	-0.06	0.00
hsCRP	0.46*	0.31	-
TNF- $\alpha$	0.47*	-	0.31

\* p < 0.01



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## Main messages

- Lean fish intake decreased blood pressure in CHD patients
- Fatty fish intake decreased lipids which are potential mediators of lipid-induced insulin resistance and inflammation.
  - IL-6 is suggested to be the link between ceramides and inflammation.

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## References

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- de Mello VDF, Lankinen M, Schwab U, Kolehmainen M, Lehto S, Oresic M, Seppänen-Laakso T, Pulkkinen L, Uusitupa M, Erkkilä AT. The link of plasma ceramides with inflammation and insulin resistance: associations with serum IL-6 concentration in patients with coronary heart disease. *Diabetologia* 2009;52:2612-2615.

*Study group at UEF:*

*Ursula Schwab  
Maria Lankinen  
Vanessa Laaksonen  
Marjukka Kolehmainen  
Leena Pulkkinen  
Mustafa Atalay  
Matti Uusitupa*

*Kuopio University Hospital:*

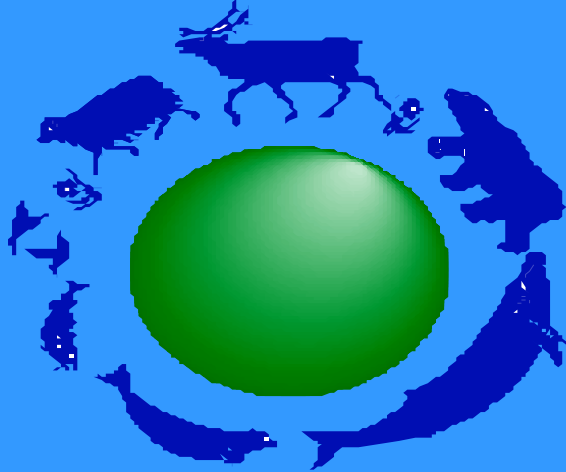
*Seppo Lehto  
Hanna Mussalo*

*VTT Technical Research Center of  
Finland:*

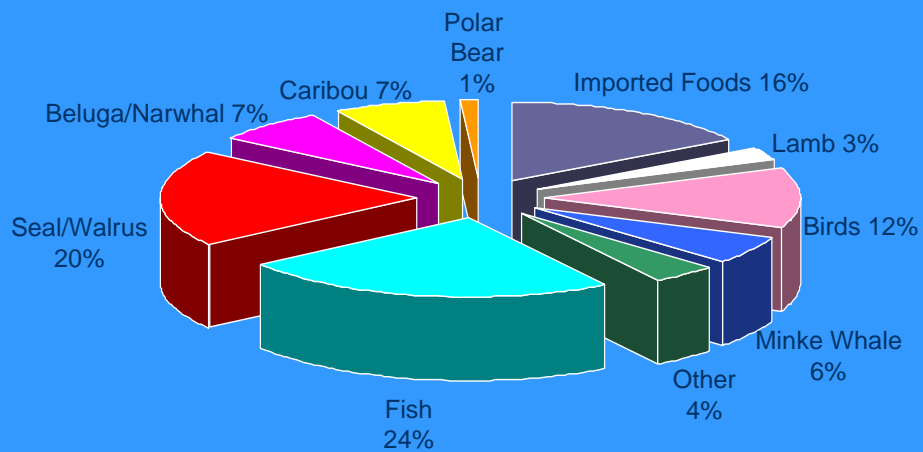
*Matej Orešič*



**Food security in the Arctic**  
**Dietary Recommendation in Greenland**  
Gert Mulvad  
Greenlandic Board of Nutrition and Environment



**Principle Meat/Fish Consumed by Selected Households**  
**in Qeqertarsuaq, 1989-1990**



## What do we eat ?

- Average in Greenland:
- 75% calorie intake from imported food.
- 25% from local country food.



## Food variation



## Drink Fresh Water



## Movement 1 hour every day



## Eat fruit and vegetables every day



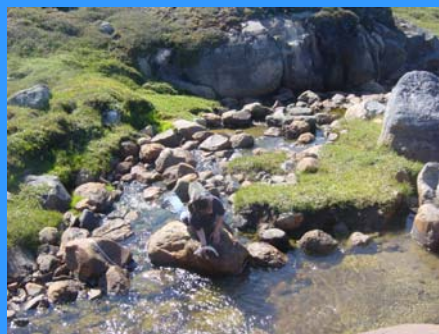
## Eat Local country food, follow the season

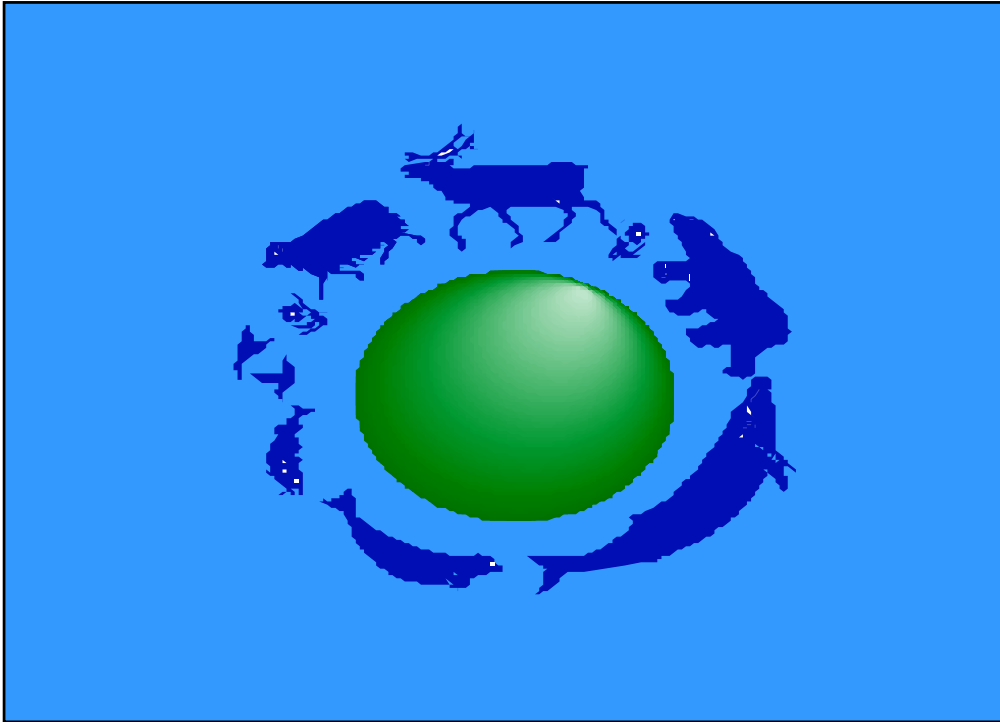


## Collecting food, preparing and eating together in the family

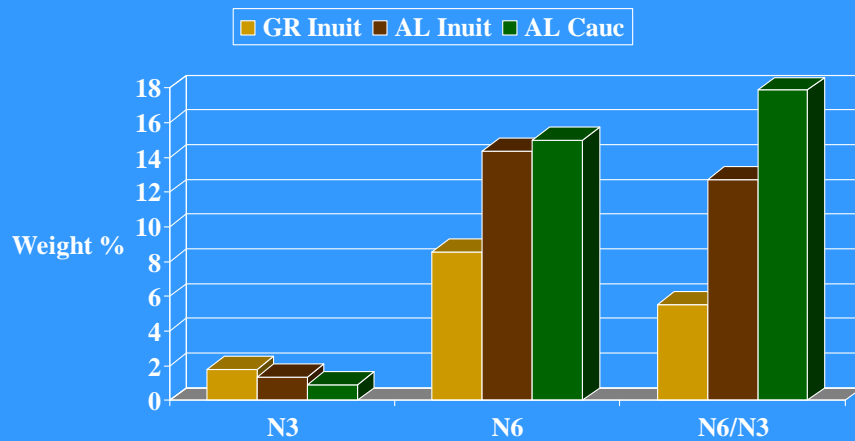


## Eat often fish.





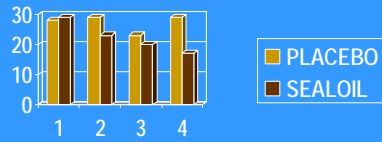
## PUFA in adipose tissue



In earlier descriptions: Especially frequent nose bleeding was seen.

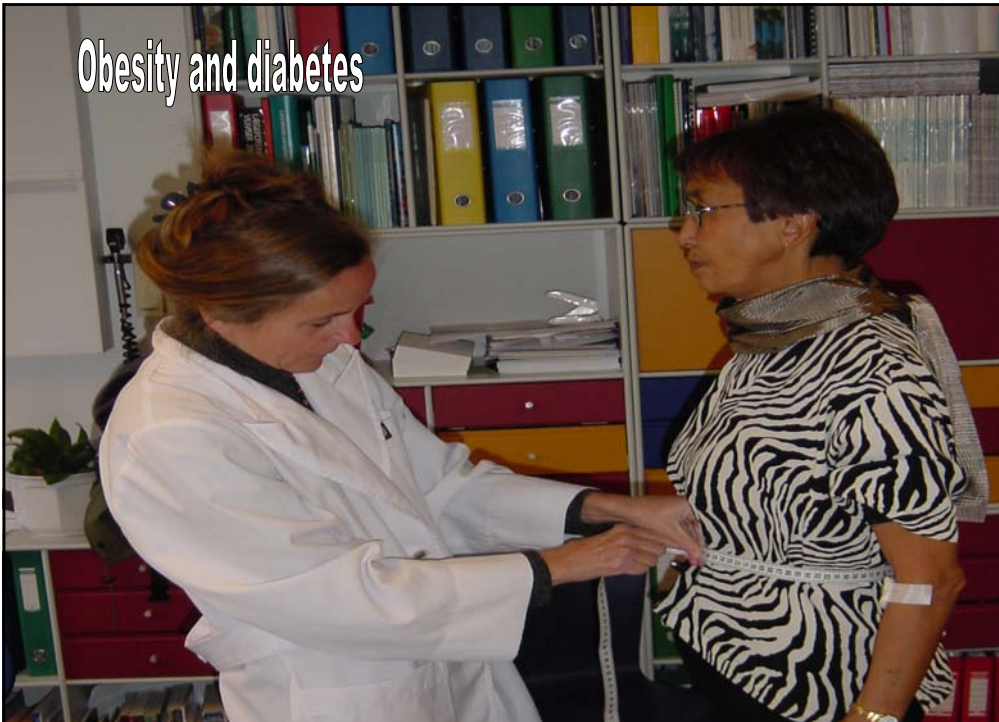


Menstrual Discomfort in Danish Women Reduced by Dietary Supplements of Omega-3 PUFA Seal Oil Capsules

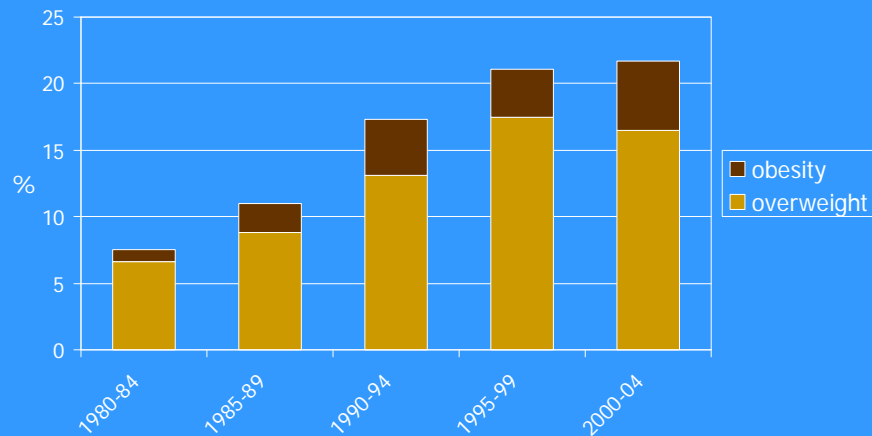


Histogram showing the change in mean number of reported menstrual symptoms As function of time ( 1= before intervention 2,3 and 4=consecutive menstrual periods During intervention.

Obesity and diabetes



## Obesity and overweight at schoolstart



Schnohr C, Sørensen TIA, Niclasen B VL. Changes since 1980 in body mass index and the prevalence of overweight among inschooling children in Nuuk, Greenland. *Int. Jr. of Circumpolar Health.*

## Subjects & Methods

- 46 Greenlanders living in Nuuk on a traditional fare.
- 45 Greenlanders living in Nuuk on a westernized fare.
- 54 Greenlanders living in Denmark on a westernized fare.
- 43 Danes living in Denmark on a westernized fare.

Blood specimens: drawn both summer and winter.

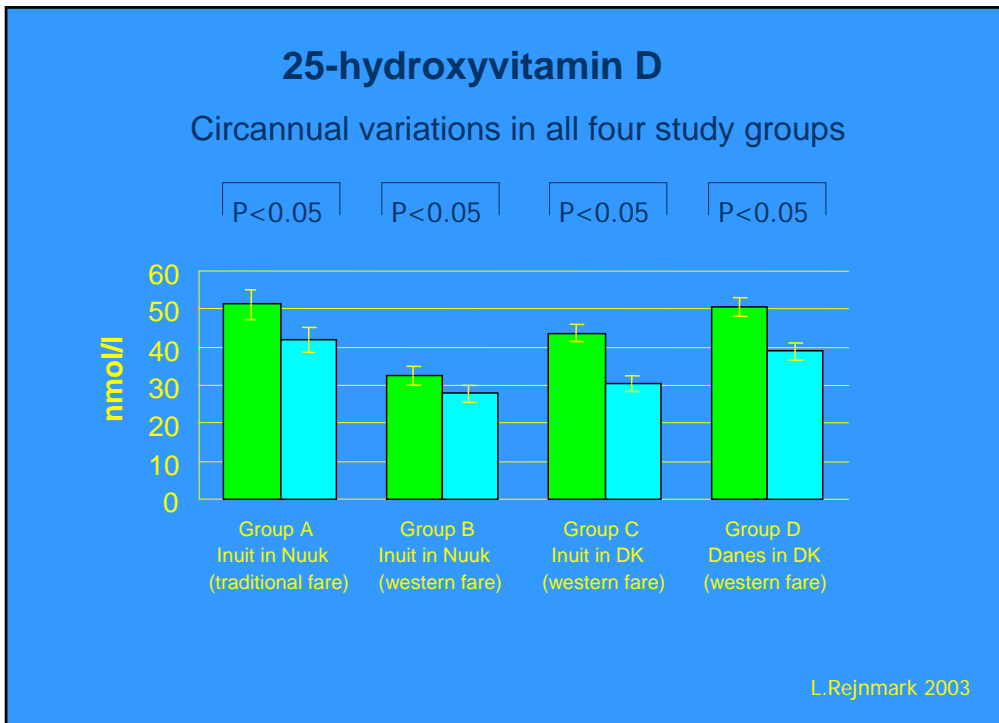
Diet:

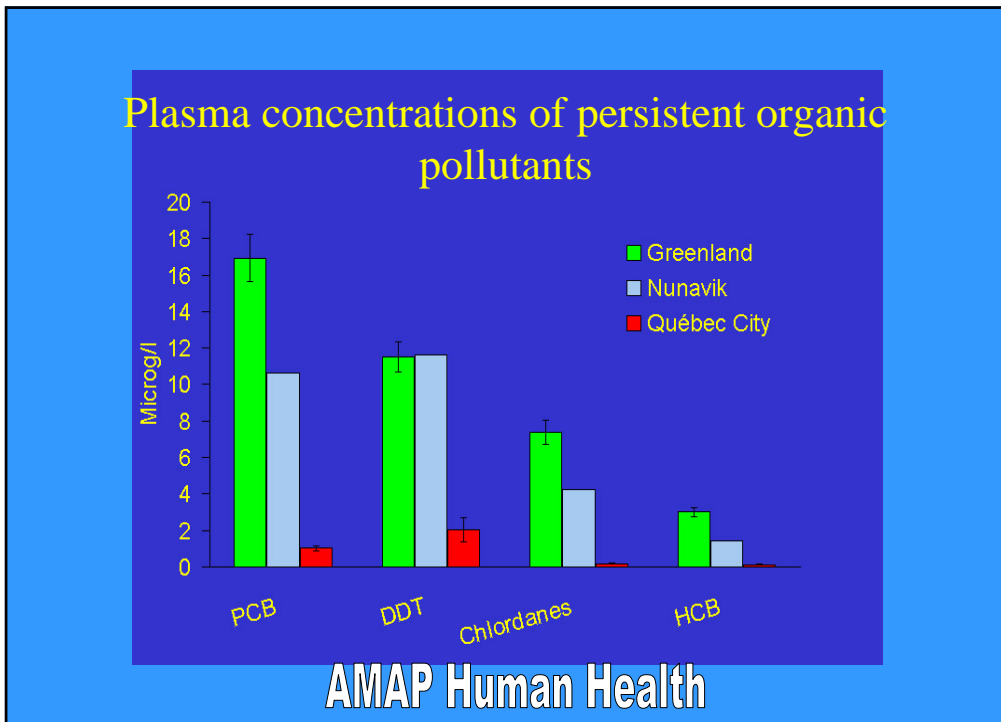
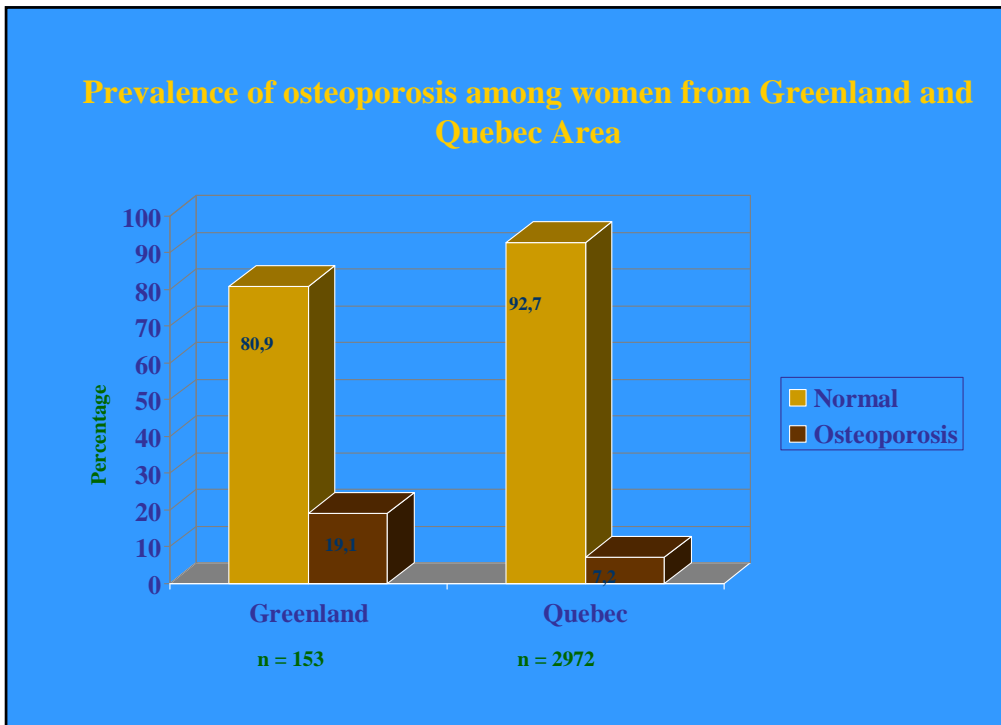
Interview based on 3-months recall

Traditional: seal and or whale at least once a week

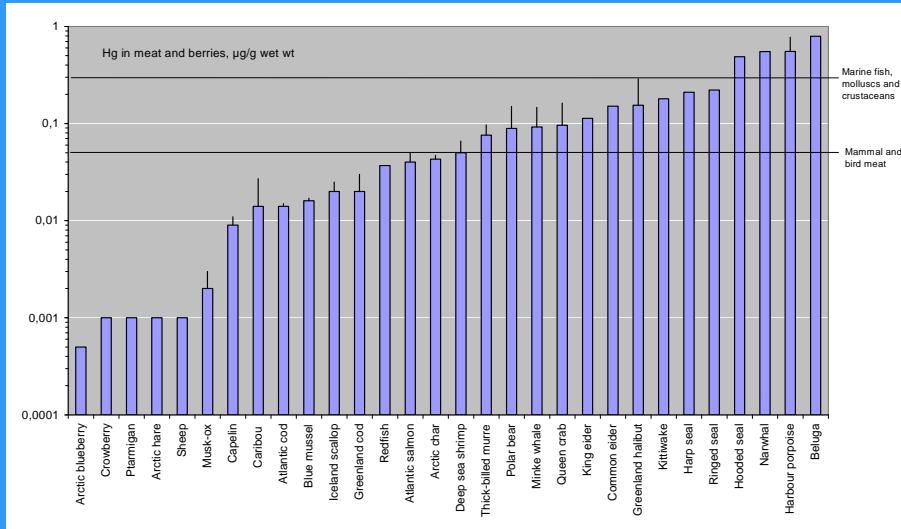
Westernized: seal and or whale < 3 times a months.

L.Rejnmark 2003

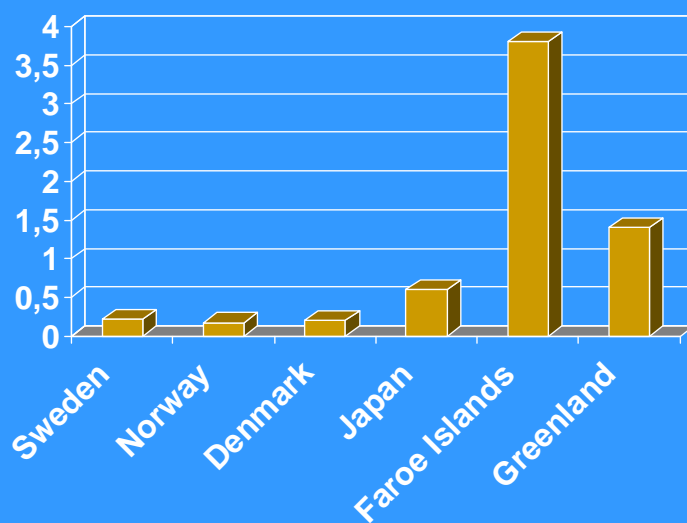




### Total mercury in the traditional Greenland diet compared to EU residue guideline values



### Mercury in human kidney (µg/g)



## Recommendation

### The Greenland Home Rule and The Greenlandic Board of Nutrition and Environment

- Problems
- Goals
- Recommendations



## Problems

- Change of diet and lifestyle toward western food means change in intake of energy, energy giving nutrition, vitamins, minerals and other biological active substances.
- Simultaneously the significance of the diet's connection to cultural, occupational and social conditions decreases.
- The Greenlandic food which is high in the food chain have problems with contamination.
- Incorrect preparation and storage of Greenlandic food can entail risk of foodborne diseases.

## Goals

- Greenlandic food subjects are included in the public institutions' food choices.
- Increased general knowledge about which food subjects that are healthy.
- Increased general knowledge about food hygiene (correct storage and handling).
- Increased general knowledge about preparation methods which foster variation and fulfil culinary and nutritional needs.

## Recommendations

- Follow the 10 food recommendation from the Greenlandic Board of Nutrition and Environment.

## Recommendations

- Local and international initiatives that lower emission of pollutants to the environment.
- Secure infrastructure which promotes the use of Greenlandic foods in homes, retail, institutions and other social settings.
- Informing and educating about food hygiene, storage and preparation of both Greenlandic and imported food.
- Guidance/educating about how Greenlandic and imported food can be included in ones diet which fulfil the nutritional recommendations.
- Local initiatives that increases security about food.

## Recommendations

- Pregnant and nursing women can continuously eat varied Greenlandic food, but should be cautious with especially polar bear, teethwhale, seabirds, aged seals. These food subjects can for instance be substituted with fish and land based mammals.
- It is recommended that children and young people follow the same advice as pregnant women. It is recommended to all that they follow the ten dietary advice devised by the Greenlandic board of Food Safety.
- There will be arranged ongoing courses which secure local knowledge on counselling and communication about Nutrition and Health.



Workshop: "Risks and Benefits of Whale and Seal Consumption" in Copenhagen 14 January 2011

## Health Benefits of Marine Mammal Based Food

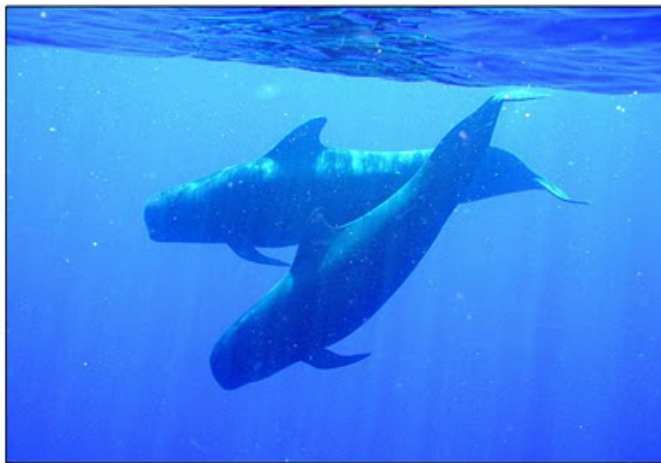
Hóraldur Joensen, Faculty of Science and Technology  
Otto Grahl Nielsen, Professor emeritus, University of Bergen



University of Faroe Islands

1

### Pilot whales



2

Killing of pilot whales

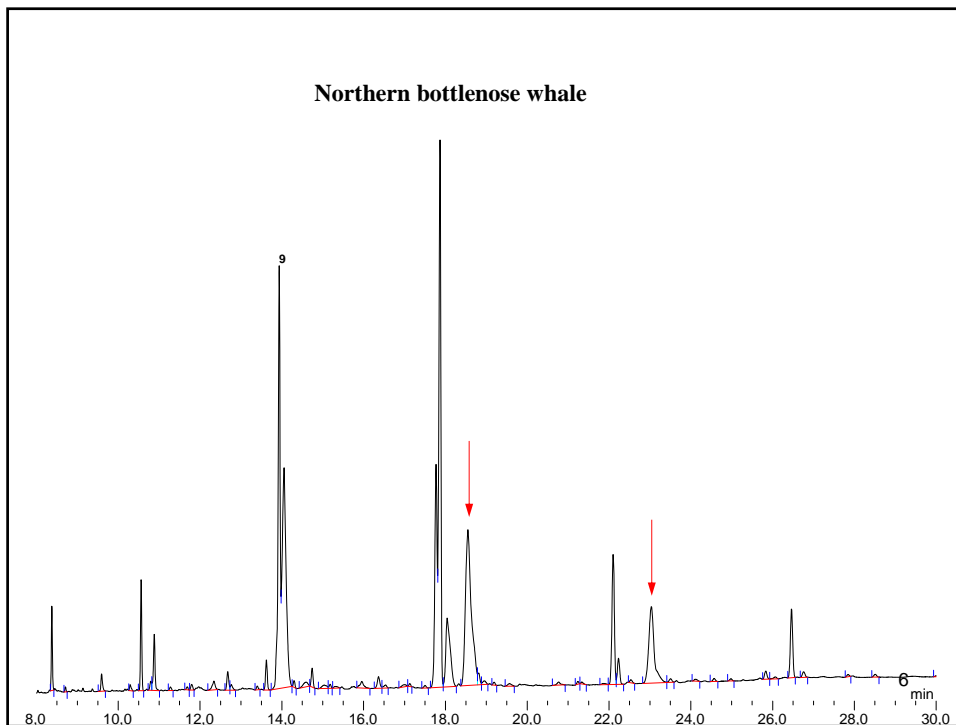
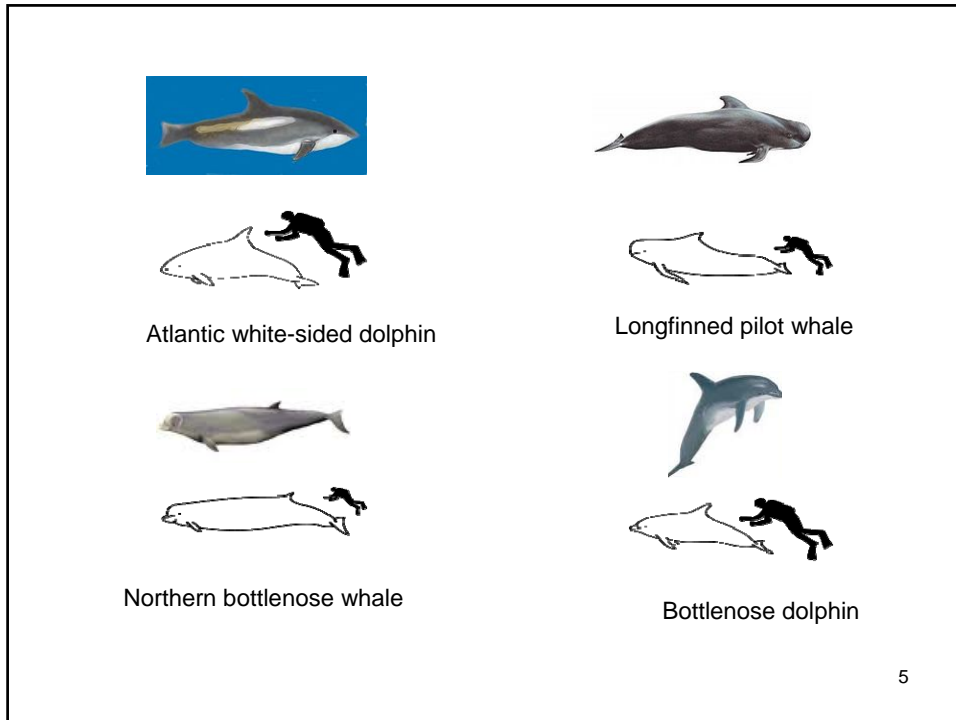


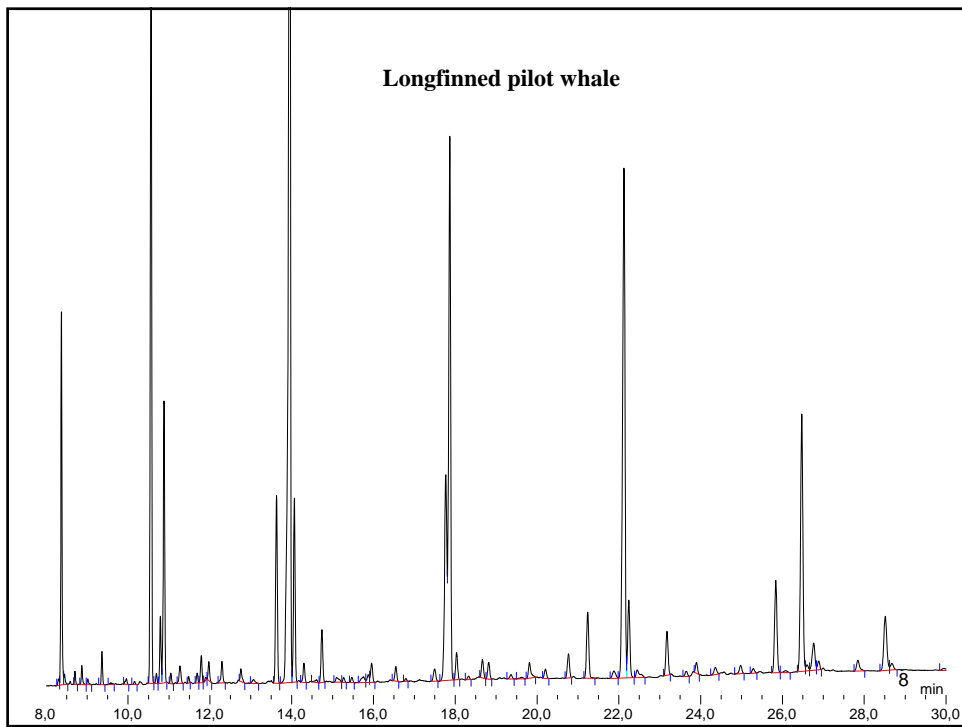
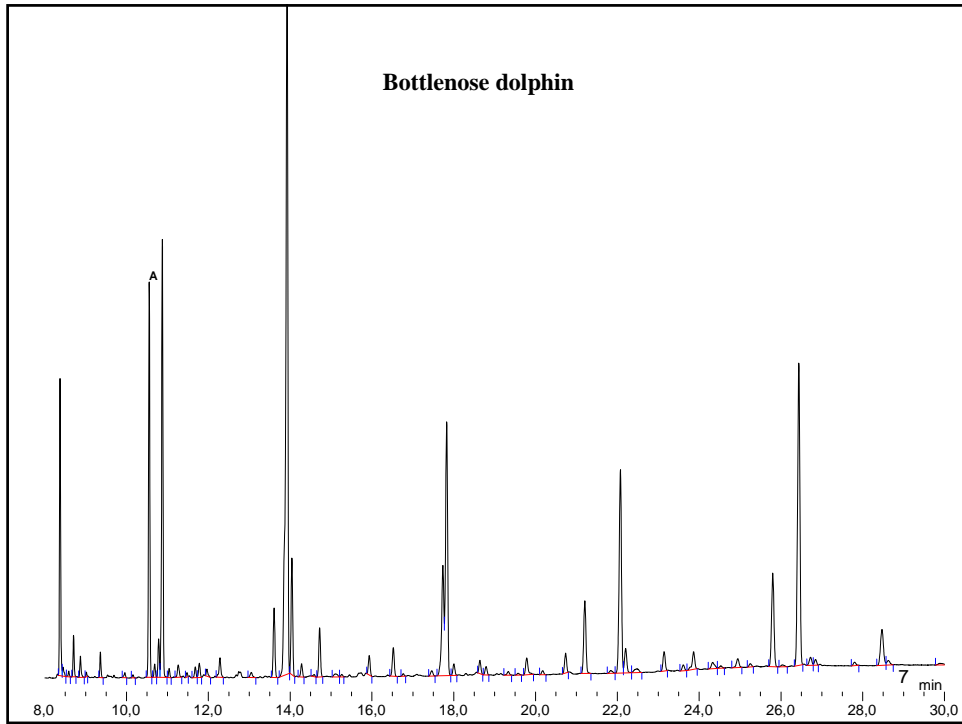
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Dish: potatoes, dried whale meat, dried fish, salted blubber



4





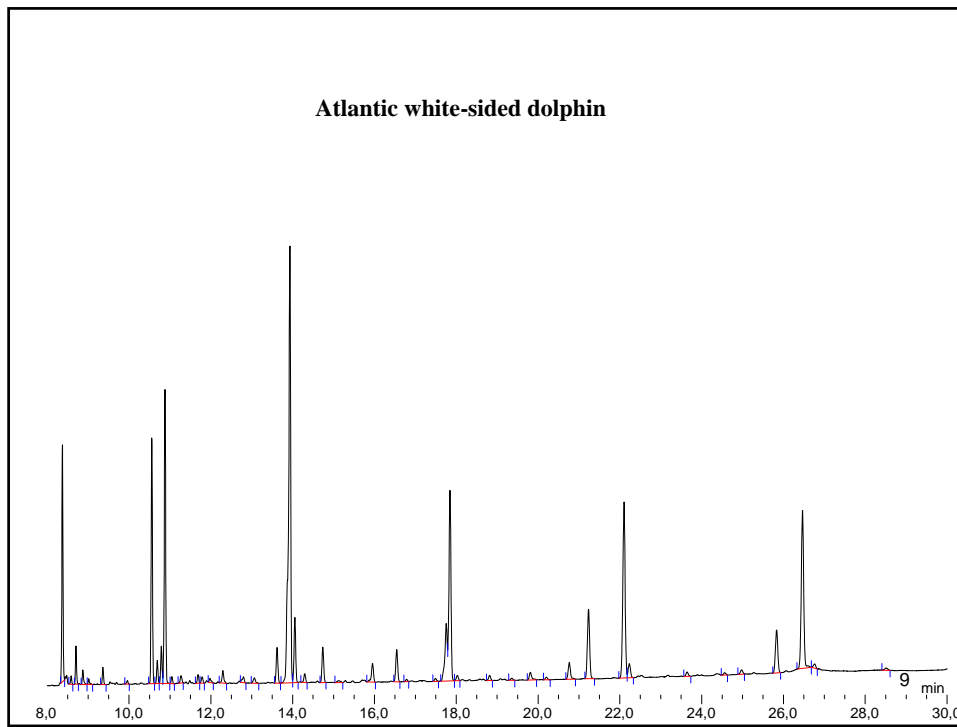
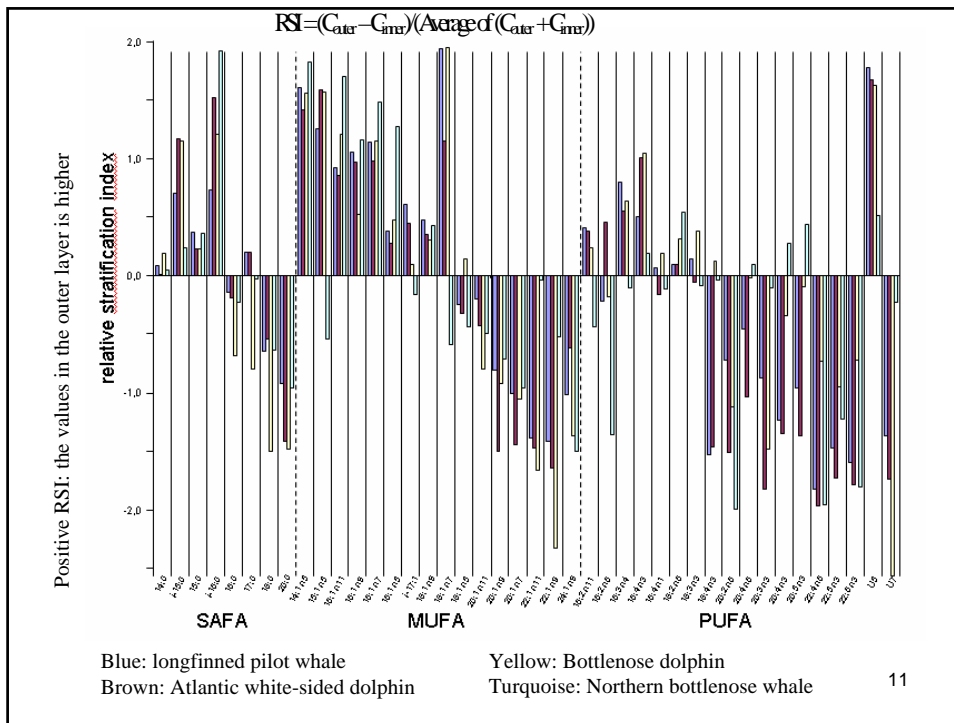


Table 1. Fatty acids in the outer and inner blubber of four whales from the waters off the Farao Islands, given as percentage of total  $\pm$  SD.

fatty acid	Longfinned pilot whale N = 5		Atlantic white-sided dolphin N = 5		Bottlenose dolphin N = 3		Northern bottlenose whale N = 3	
	outer blubber	inner blubber	outer blubber	inner blubber	outer blubber	inner blubber	outer blubber	inner blubber
14:0	4.8 $\pm$ 0.5	4.4 $\pm$ 0.4	6.2 $\pm$ 0.6	6.2 $\pm$ 0.4	5.5 $\pm$ 0.4	5.6 $\pm$ 0.2	1.5 $\pm$ 0.2	1.4 $\pm$ 0.1
14:1n5	1.6 $\pm$ 0.4	0.2 $\pm$ 0.0	6.0 $\pm$ 1.2	1.0 $\pm$ 0.4	3.3 $\pm$ 0.6	0.7 $\pm$ 0.5	1.9 $\pm$ 0.1	0.1 $\pm$ 0.0
i-15:0	0.6 $\pm$ 0.1	0.3 $\pm$ 0.0	1.8 $\pm$ 0.3	0.5 $\pm$ 0.1	1.3 $\pm$ 0.5	0.4 $\pm$ 0.0	0.1 $\pm$ 0.0	0.1 $\pm$ 0.0
15:0	0.6 $\pm$ 0.0	0.4 $\pm$ 0.0	0.6 $\pm$ 0.1	0.4 $\pm$ 0.0	0.5 $\pm$ 0.1	0.4 $\pm$ 0.0	0.1 $\pm$ 0.0	0.1 $\pm$ 0.0
15:1n5	0.2 $\pm$ 0.1	0.0 $\pm$ 0.0	0.7 $\pm$ 0.1	0.1 $\pm$ 0.1	0.5 $\pm$ 0.2	0.1 $\pm$ 0.0	0.3 $\pm$ 0.0	0.5 $\pm$ 0.1
i-16:0	0.3 $\pm$ 0.1	0.1 $\pm$ 0.0	1.1 $\pm$ 0.3	0.2 $\pm$ 0.0	0.5 $\pm$ 0.3	0.1 $\pm$ 0.0	0.1 $\pm$ 0.0	0.0 $\pm$ 0.0
16:0	10.3 $\pm$ 1.0	11.8 $\pm$ 0.7	6.0 $\pm$ 1.0	7.3 $\pm$ 0.6	6.2 $\pm$ 1.6	8.9 $\pm$ 1.9	1.7 $\pm$ 0.2	2.2 $\pm$ 0.1
16:1n11	0.4 $\pm$ 0.1	0.2 $\pm$ 0.0	1.7 $\pm$ 0.2	0.7 $\pm$ 0.2	0.9 $\pm$ 0.3	0.3 $\pm$ 0.1	0.5 $\pm$ 0.1	0.0 $\pm$ 0.0
16:1n9	3.0 $\pm$ 0.3	0.9 $\pm$ 0.1	3.2 $\pm$ 0.5	1.1 $\pm$ 0.3	1.6 $\pm$ 0.3	0.7 $\pm$ 0.2	1.0 $\pm$ 0.1	0.3 $\pm$ 0.0
16:1n7	15.3 $\pm$ 1.3	4.2 $\pm$ 0.4	26.8 $\pm$ 2.0	9.1 $\pm$ 1.8	20.3 $\pm$ 3.1	8.1 $\pm$ 2.2	8.8 $\pm$ 0.3	1.3 $\pm$ 0.2
16:1n5	0.2 $\pm$ 0.0	0.2 $\pm$ 0.0	0.3 $\pm$ 0.0	0.2 $\pm$ 0.0	0.3 $\pm$ 0.0	0.2 $\pm$ 0.0	0.1 $\pm$ 0.0	0.0 $\pm$ 0.0
16:2n11	0.6 $\pm$ 0.1	0.4 $\pm$ 0.0	0.5 $\pm$ 0.1	0.4 $\pm$ 0.0	0.5 $\pm$ 0.1	0.4 $\pm$ 0.0	0.1 $\pm$ 0.0	0.1 $\pm$ 0.0
16:2n6	0.1 $\pm$ 0.0	0.1 $\pm$ 0.0	0.2 $\pm$ 0.0	0.1 $\pm$ 0.0	0.1 $\pm$ 0.0	0.1 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
i-17:1	0.7 $\pm$ 0.1	0.4 $\pm$ 0.1	0.4 $\pm$ 0.1	0.3 $\pm$ 0.0	0.4 $\pm$ 0.1	0.3 $\pm$ 0.0	0.1 $\pm$ 0.1	0.1 $\pm$ 0.0
17:0	0.5 $\pm$ 0.0	0.4 $\pm$ 0.0	0.2 $\pm$ 0.1	0.2 $\pm$ 0.0	0.2 $\pm$ 0.1	0.3 $\pm$ 0.0	0.2 $\pm$ 0.1	0.2 $\pm$ 0.0
16:3n4	1.1 $\pm$ 0.1	0.5 $\pm$ 0.0	0.9 $\pm$ 0.1	0.5 $\pm$ 0.1	0.9 $\pm$ 0.1	0.5 $\pm$ 0.1	0.4 $\pm$ 0.0	0.5 $\pm$ 0.1
16:4n3	0.5 $\pm$ 0.0	0.3 $\pm$ 0.0	1.0 $\pm$ 0.2	0.3 $\pm$ 0.1	0.9 $\pm$ 0.0	0.2 $\pm$ 0.1	0.3 $\pm$ 0.0	0.2 $\pm$ 0.0
16:4n1	0.2 $\pm$ 0.0	0.1 $\pm$ 0.0	0.2 $\pm$ 0.0	0.3 $\pm$ 0.0	0.2 $\pm$ 0.0	0.2 $\pm$ 0.0	0.1 $\pm$ 0.0	0.1 $\pm$ 0.0
18:0	1.7 $\pm$ 0.2	3.4 $\pm$ 0.3	0.7 $\pm$ 0.2	1.3 $\pm$ 0.1	1.1 $\pm$ 0.1	2.0 $\pm$ 0.5	0.4 $\pm$ 0.0	0.8 $\pm$ 0.0
18:1n9	37.2 $\pm$ 1.3	22.8 $\pm$ 2.2	29.2 $\pm$ 1.2	20.5 $\pm$ 2.1	30.6 $\pm$ 1.9	20.7 $\pm$ 3.6	20.4 $\pm$ 1.5	13.2 $\pm$ 0.9
18:1n7	3.1 $\pm$ 0.8	0.0 $\pm$ 0.0	1.6 $\pm$ 0.6	0.4 $\pm$ 0.9	3.4 $\pm$ 0.2	0.0 $\pm$ 0.0	7.1 $\pm$ 0.5	13.0 $\pm$ 0.9
18:1n5	0.3 $\pm$ 0.1	0.3 $\pm$ 0.0	0.3 $\pm$ 0.0	0.4 $\pm$ 0.0	0.4 $\pm$ 0.0	0.4 $\pm$ 0.0	0.2 $\pm$ 0.0	0.3 $\pm$ 0.0
18:2n6	1.0 $\pm$ 0.1	0.9 $\pm$ 0.0	1.5 $\pm$ 0.1	1.3 $\pm$ 0.1	1.3 $\pm$ 0.2	1.3 $\pm$ 0.1	1.1 $\pm$ 0.0	0.6 $\pm$ 0.0
18:3n3	0.5 $\pm$ 0.1	0.4 $\pm$ 0.0	0.8 $\pm$ 0.1	0.8 $\pm$ 0.1	0.7 $\pm$ 0.1	0.8 $\pm$ 0.1	0.5 $\pm$ 0.0	0.5 $\pm$ 0.0
18:4n3	0.1 $\pm$ 0.0	0.4 $\pm$ 0.1	0.2 $\pm$ 0.1	1.4 $\pm$ 0.2	0.4 $\pm$ 0.2	1.3 $\pm$ 0.6	0.1 $\pm$ 0.1	0.2 $\pm$ 0.0
20:0	0.1 $\pm$ 0.0	0.2 $\pm$ 0.0	0.0 $\pm$ 0.0	0.1 $\pm$ 0.0	0.1 $\pm$ 0.0	0.2 $\pm$ 0.0	0.0 $\pm$ 0.0	0.1 $\pm$ 0.0
20:1n11	4.3 $\pm$ 0.4	5.2 $\pm$ 0.4	2.0 $\pm$ 0.4	3.1 $\pm$ 0.5	3.0 $\pm$ 0.6	3.8 $\pm$ 0.4	4.7 $\pm$ 0.2	7.9 $\pm$ 0.3
20:1n9	4.5 $\pm$ 0.4	10.5 $\pm$ 0.6	1.4 $\pm$ 0.6	9.6 $\pm$ 1.4	4.7 $\pm$ 1.3	8.4 $\pm$ 0.7	8.9 $\pm$ 0.5	18.8 $\pm$ 1.5
20:1n7	0.2 $\pm$ 0.0	0.6 $\pm$ 0.0	0.1 $\pm$ 0.1	0.3 $\pm$ 0.1	0.2 $\pm$ 0.1	0.4 $\pm$ 0.1	1.7 $\pm$ 0.2	4.8 $\pm$ 0.1
U5	0.8 $\pm$ 0.3	0.0 $\pm$ 0.1	0.5 $\pm$ 0.2	0.0 $\pm$ 0.0	0.4 $\pm$ 0.2	0.1 $\pm$ 0.0	25.8 $\pm$ 1.3	15.2 $\pm$ 1.1
20:2n6	0.2 $\pm$ 0.0	0.4 $\pm$ 0.0	0.0 $\pm$ 0.0	0.2 $\pm$ 0.0	0.2 $\pm$ 0.0	0.3 $\pm$ 0.0	0.0 $\pm$ 0.0	0.5 $\pm$ 0.1
20:4n6	0.3 $\pm$ 0.1	0.5 $\pm$ 0.0	0.1 $\pm$ 0.0	0.4 $\pm$ 0.0	0.5 $\pm$ 0.1	0.6 $\pm$ 0.1	0.1 $\pm$ 0.0	0.1 $\pm$ 0.1
20:3n3	0.1 $\pm$ 0.0	0.2 $\pm$ 0.0	0.0 $\pm$ 0.0	0.1 $\pm$ 0.0	0.1 $\pm$ 0.0	0.1 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
20:4n3	0.1 $\pm$ 0.0	0.6 $\pm$ 0.2	0.2 $\pm$ 0.1	0.9 $\pm$ 0.1	0.4 $\pm$ 0.2	0.9 $\pm$ 0.3	0.2 $\pm$ 0.1	0.2 $\pm$ 0.0
20:5n3	0.7 $\pm$ 0.2	2.0 $\pm$ 0.7	0.8 $\pm$ 0.3	4.0 $\pm$ 0.4	1.5 $\pm$ 0.8	3.8 $\pm$ 1.8	0.3 $\pm$ 0.1	0.2 $\pm$ 0.0
22:1n11	2.2 $\pm$ 0.4	12.1 $\pm$ 0.8	1.6 $\pm$ 1.0	10.3 $\pm$ 2.6	2.6 $\pm$ 0.8	8.8 $\pm$ 1.7	5.2 $\pm$ 0.5	5.4 $\pm$ 0.9
22:1n9	0.3 $\pm$ 0.1	1.7 $\pm$ 0.2	0.1 $\pm$ 0.0	1.0 $\pm$ 0.2	0.3 $\pm$ 0.1	1.0 $\pm$ 0.2	0.6 $\pm$ 0.1	1.0 $\pm$ 0.1
U7a	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.1	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	5.0 $\pm$ 0.5	6.2 $\pm$ 0.6
22:4n6	0.0 $\pm$ 0.0	0.3 $\pm$ 0.0	0.0 $\pm$ 0.0	0.3 $\pm$ 0.1	0.1 $\pm$ 0.1	0.4 $\pm$ 0.1	0.0 $\pm$ 0.0	0.1 $\pm$ 0.0
22:5n3	0.5 $\pm$ 0.1	3.2 $\pm$ 0.7	0.3 $\pm$ 0.1	3.5 $\pm$ 0.8	1.0 $\pm$ 0.5	3.8 $\pm$ 0.4	0.1 $\pm$ 0.0	0.4 $\pm$ 0.0
22:6n3	1.0 $\pm$ 0.3	8.7 $\pm$ 2.2	0.6 $\pm$ 0.4	10.7 $\pm$ 1.2	3.0 $\pm$ 2.0	13.0 $\pm$ 1.5	0.1 $\pm$ 0.1	2.8 $\pm$ 1.2
24:1n9	0.2 $\pm$ 0.1	0.5 $\pm$ 0.1	0.1 $\pm$ 0.0	0.3 $\pm$ 0.1	0.1 $\pm$ 0.1	0.3 $\pm$ 0.1	0.1 $\pm$ 0.0	0.1 $\pm$ 0.0



### Health Benefits of Omega-3

Natural hormone replacement

Nervous system

Immune system

Helps to suppress appetite

Helps to burn stored body fat

Brain function

Eysight

Healthy skin

Joints

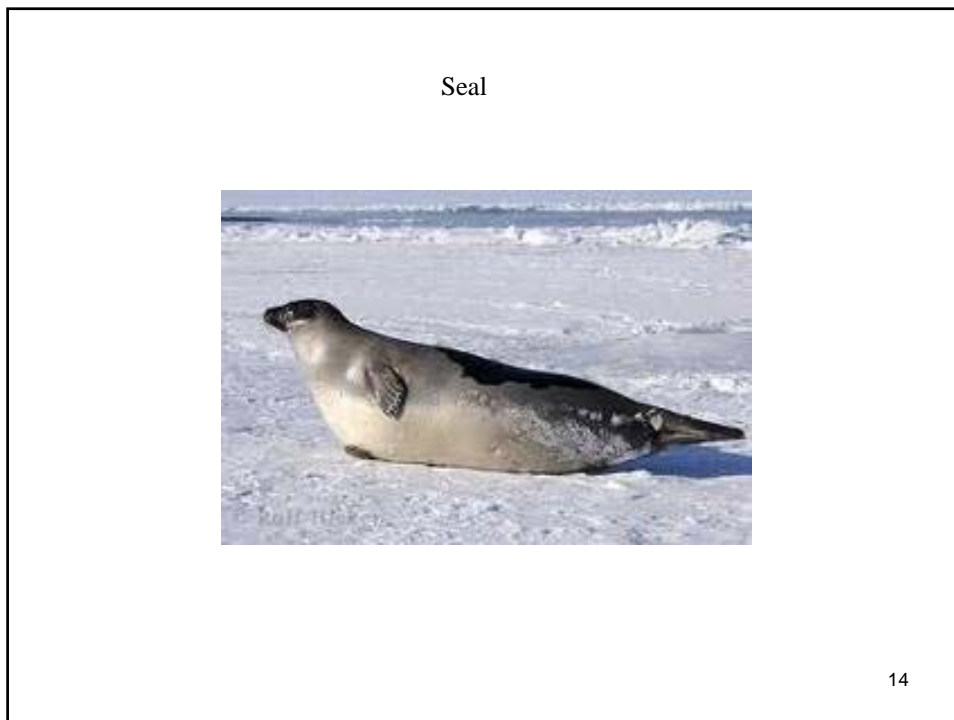
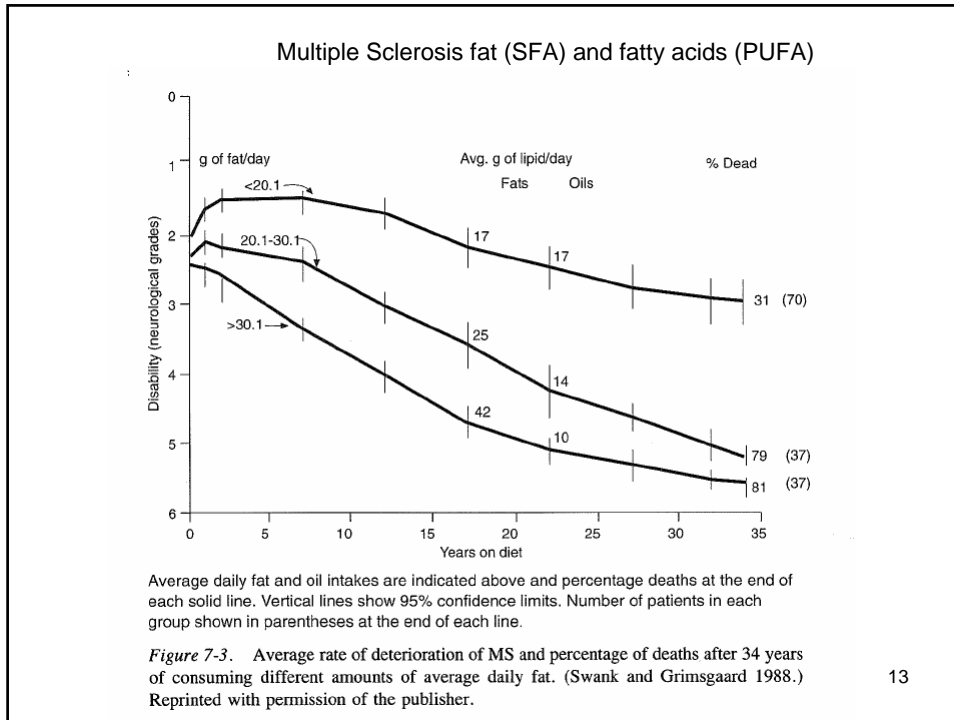
Reduces inflammation related to many diseases

Important for pregnant women and nursing mothers

Heart

Liver (cholesterol levels)

12



Nutritional composition of blubber and meat of hooded seal and harp seal From Greenland (Brunborg et al. 2005)

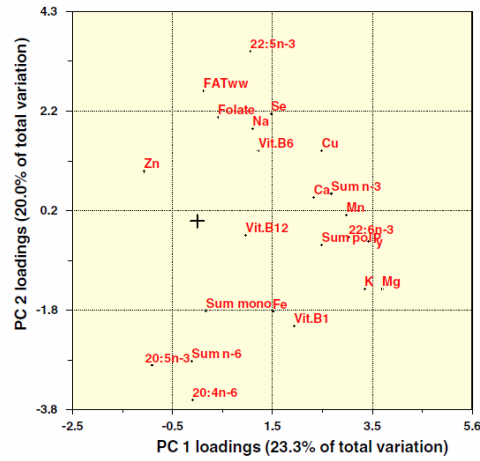
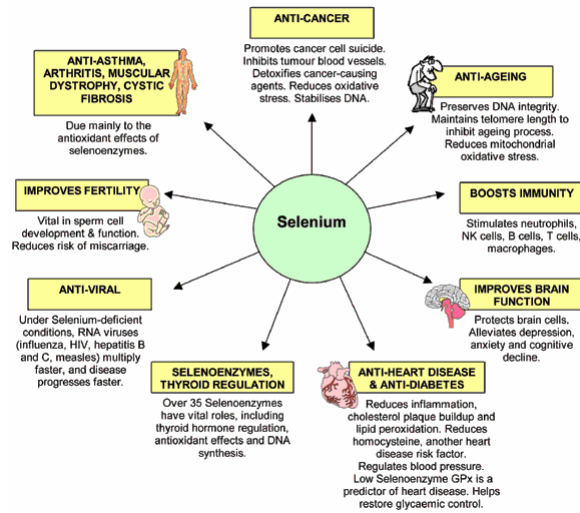


Fig. 2. Loadings from the corresponding PCA model in Fig. 1, showing the correlation between some selected fatty acids, B-vitamins, minerals and trace-elements.

15

The Health Benefits of Selenium.



16

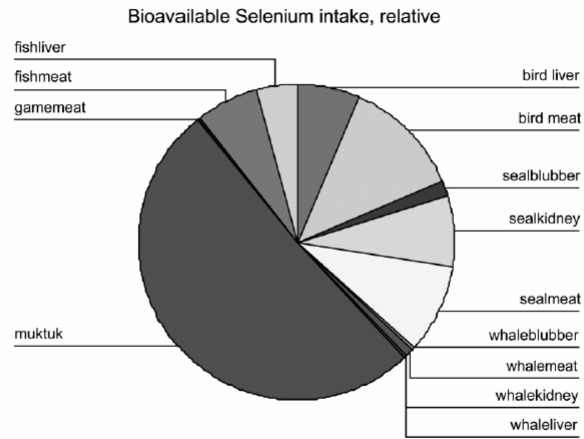


Fig. 2. The relative contributions of various food items to bioavailable Se (total selenium minus mercury bound) intake in a West Greenland population,  $n = 200$ .

### Selenium's importance in regulatory issues regarding mercury

Laura J. Raymond\*, Nicholas V.C. Ralston Fuel Processing Technology 90 (2009) 1333–1338  
University of North Dakota Energy & Environmental Research Center, 15 North 23rd Street, Stop 9018, Grand Forks, ND 58202-9018, United States

Since blood mercury levels reflect mercury exposure from fish consumption but do not provide a reliable indication of the risks associated with mercury exposure, it has become clear that a new seafood safety criterion is needed. Risks of mercury exposure are directly related to molar ratios of Hg:Se in proportion to the absolute amounts of mercury and selenium present in the seafoods. In order to integrate selenium-specific nutritional benefits in relation to potential mercury exposure risks presented by consumption of a given type of seafood, a comprehensive index known as the Se-HBV has been created. It is calculated as follows:

$$\text{Se - HBV} = (\text{Se : Hg molar ratio} \times \text{total Se}) - (\text{Hg : Se molar ratio} \times \text{total Hg})$$

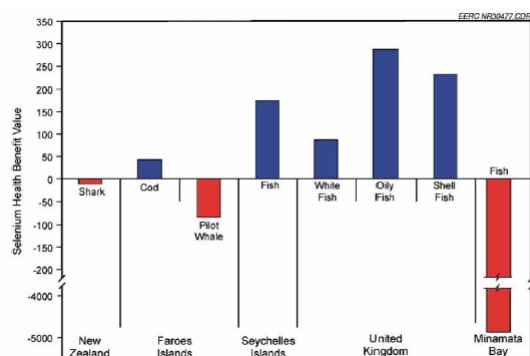
Most ocean fish have highly positive Se-HBVs because they are rich sources of dietary selenium, which is usually present in far greater molar quantities than methylmercury. This explains why experi-

## Selenium's importance in regulatory issues regarding mercury

Laura J. Raymond\*, Nicholas V.C. Ralston

Fuel Processing Technology 90 (2009) 1333–1338

University of North Dakota Energy &amp; Environmental Research Center, 15 North 23rd Street, Stop 9018, Grand Forks, ND 58202-9018, United States



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## Major Bioactivities of Marine Peptides

- Antihypertensive (ACE inhibitory) activity
- Antioxidant activity
- Antimicrobial activity
- Antiviral activity
- Anticancerogenic
- Obesity control
- Calcium-Binding activity
- Immunostimulating activity
- Osteoporosis alleviating
- HIV-I protease inhibiting activity
- Growth promoting

20

### Epigenetic inheritance

Dutch Winter Famine 1944/45; food?, lack of food has a transgenerational impact

Endocrinology, January 2010, 151(1):7-13 endo.endojournals.org 11

#### Transgenerational Programming of HPA Function

Matthews and Phillips, 2010 21

Hypothalamo-Pituitary-Adrenal axis, HPA axis, and associated neurocrine changes form at key component of the response of the organism to stressful challenges.

22

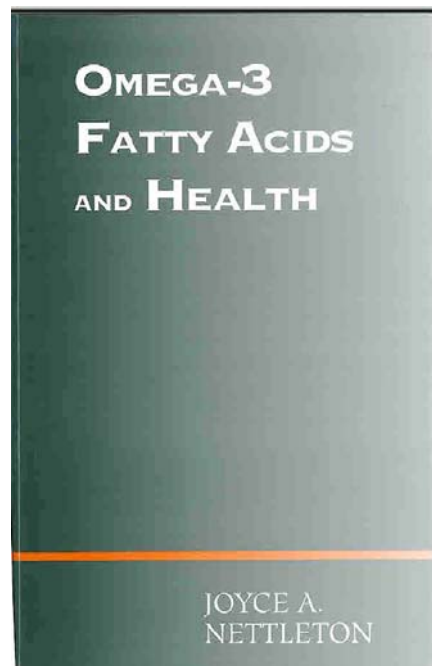
## Future studies in marine mammals raw and cooked

- Measure vitamins, macrominerals, trace-minerals, lipid-classis, fatty acids, carnitin, taurine, selen i different species seasonally
- Study bioactive peptides in fresh, light to heavy fermented and dry whale and seal meet, different species seasonally
- Food and health relations in children, youth, adults, the elderly

23

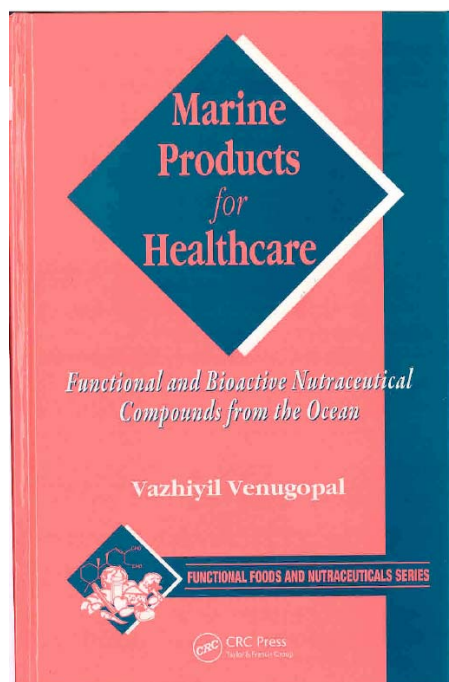
## Reviews

Year 1995. Pages: 359



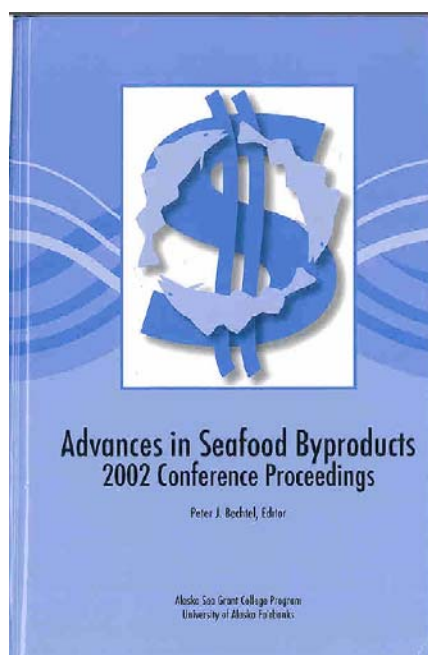
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Year 2009. Pages: 527



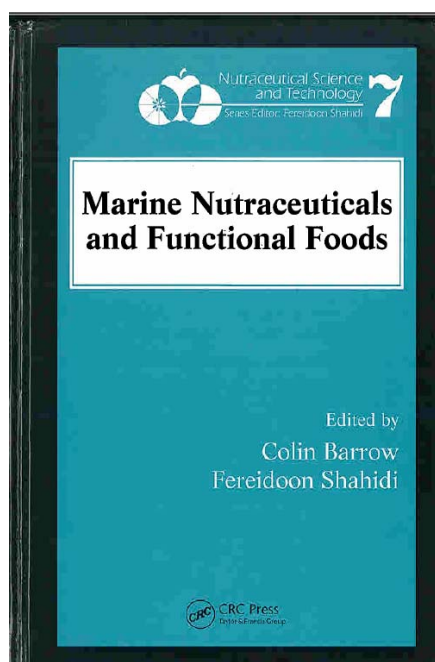
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Year 2002. Pages: 556



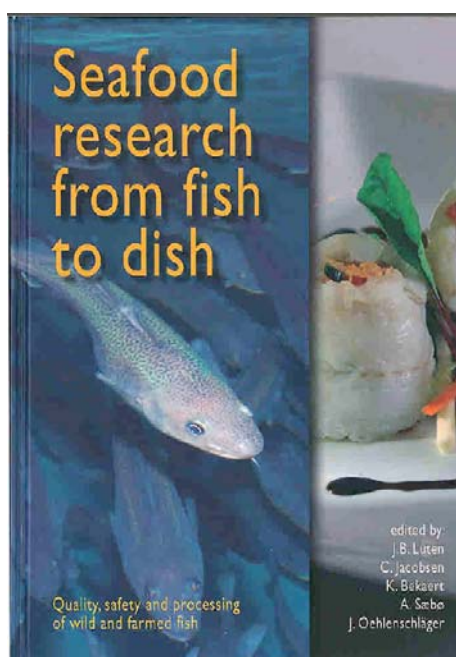
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Year 2008. Pages: 494



27

Year 2006. Pages: 567



28

Thanks  
for your  
attention



University of Faroe Islands