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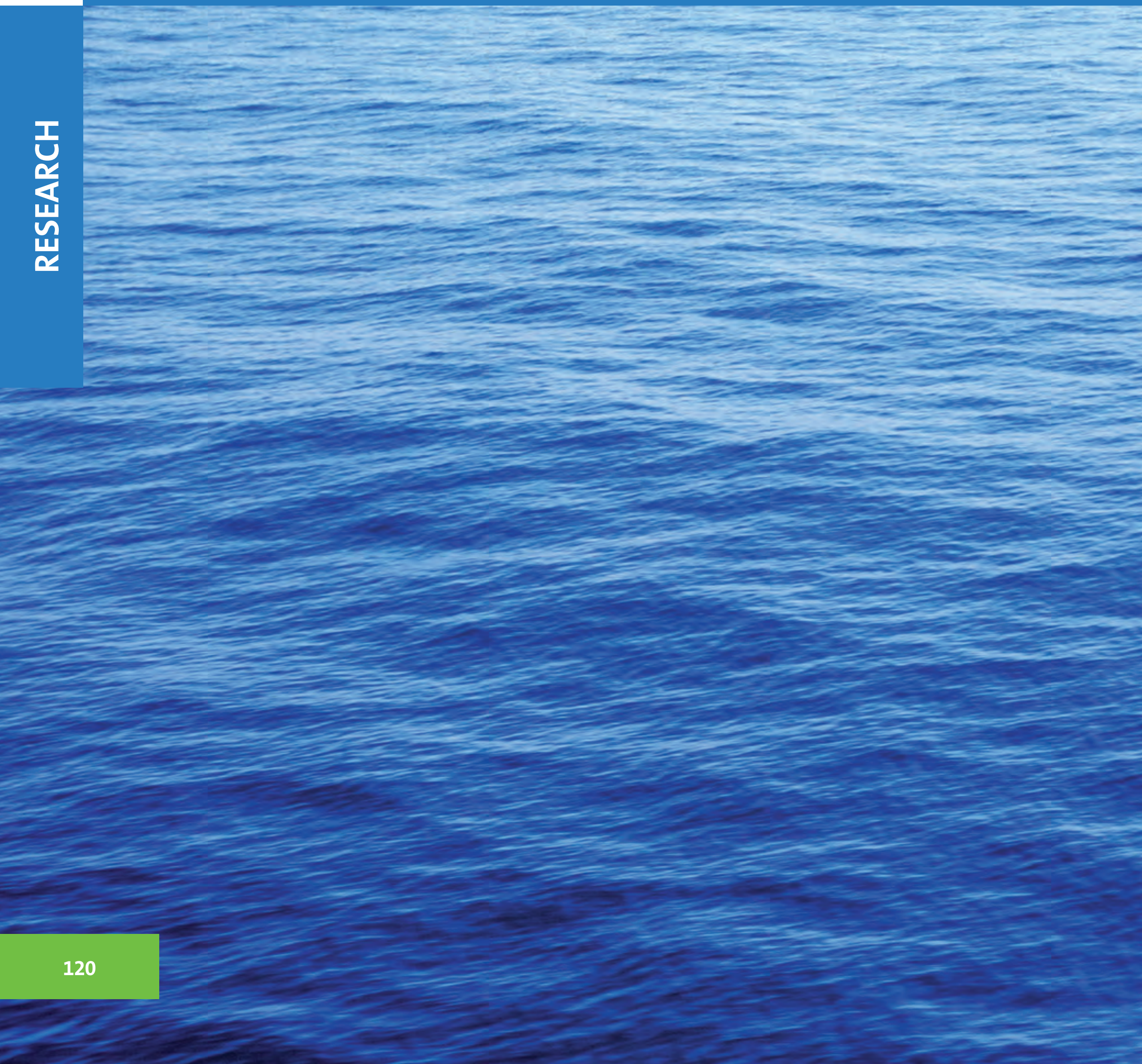
Olli Leino

Fish consumption: human health effects and decision making



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Fish consumption: human health effects and decision making

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Dedicated to Muska

Abstract

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Majority of the scientific literature suggest that fish consumption is good for human health. However, there are also opposing opinions, and assessment results are sometimes confusing. This work tries to bring understanding to these controversies by focusing on three areas: 1) scientific information on fish consumption and health 2) choosing assessment method (i.e. framework), 3) other interests and valuations related to research questions. These three domains form the decision support. Together with fish consumption mediated health effects, related decision making is the main interest in this thesis.

At the European standards, Finland can be considered as a high fish consumption country. Moreover, intake of omega-3 fatty acids in Finland mainly comes from fish consumption, and there is good evidence that intake of omega-3 fatty acids reduce risk of both cardiovascular diseases and improve development of nervous system in children. There are three predominant contaminants found in fish in Finland: methylmercury (MeHg), dioxins, and PCBs. MeHg biomagnify in food chain, and nervous system is the target tissue. Especially children are vulnerable to adverse effect of MeHg exposure. Dioxins accumulate in fat tissue and they are also very persistent. Because fish in the Baltic Sea is contaminated with dioxins and PCBs, these two substances are of special concern in Finland.

Choosing the assessment method is a critical phase because need and purpose should determine what method is used in an assessment. It is also important to understand what interests are involved in the assessment process because it affects which method best fulfills the purpose of the assessment. Guidance value assessments tend to have narrower scope, and therefore they are practical for regulative purposes. Risk assessments take a step further in estimating probability of health effects due to exposures, and in comparative risk assessments two or more risks are compared with each other. Both risk assessments and comparative risk assessments provide useful information for the decision making. Benefit-risk assessments are able to capture the net health effects of intake of a whole food item, rather than from a single substance, which makes it particularly useful for food health impact assessments. However, benefits and risk are assessed differently which is a source of bias in benefit-risk assessments. Nevertheless, benefit assessment is an essential part in the decision making related to fish consumption.

An additional challenge is that the health end points are often very different in nature, and comparing incommensurable health endpoints is a subject of valuations. Common metric approach can aggregate different health endpoints into a single number which makes it an efficient tool to be used in the decision making.

Behind the scientific information and assessment methods, there are valuations and interests which are potentially relevant inputs to decision support. In this work, these are called other interests. Other interests can be understood as both societal and individual valuations. At the individual level, these often manifest as perceptions, emotional and psychological outcomes of risk information. Feeling of threat is typically the major contributor of risk perception. Including other interests may provide additional value to the societal decision making. Importantly, other interests and perceptions often affect the whole assessment process chain, from the beginning to the end. Similarly, in choosing the assessment method, purpose and need of the assessment should also determine which interests are included. Typically, less weight on other interests is given in narrow scoped and regulatory type of assessments, whereas more weight is given in assessment approaches where participation is involved.

The original publications of this thesis confirmed that fish consumption in Finland does not pose major health risks for the general population. Rather, potential health benefits can be gained following the national fish consumption recommendation. The publications also suggest that te health benefits and risks are highly dependent on age group (e.g. children), and which fish species are consumed. The potential adverse health effects of mercury exposure are mainly due to consumption of domestic freshwater predator fish species, whereas dioxins mainly accumulate to humans from consumption of wild marine (fatty) fish species.

The ambiguities make communicating fish consumption mediated risks and benefits very delicate matters, and therefore special attention should be paid to understanding consumer perceptions and risk communication. The use of various different assessment methods brings additional ambiguity to the issue because choosing the assessment method and scoping the assessment may already determine the outcome of the assessment. Identifying the roles of the three domains presented in this work (scientific information, choosing the assessment method, other interests) brings additional value to the decision making.

Keywords: fish consumption, health, risk, benefit, assessment, decision making

Tiivistelmä

Olli Leino, Kalan syönnin terveysvaikutukset ja päätöksenteko, Terveyden ja hyvinvoinnin laitos. Tutkimus 120_2014. Helsinki, Finland 2014.
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Eri terveysvaikutusarviointien johtopäätökset voivat olla epäselviä tai keskenään ristiriitaisia. Kalan syöntiin sisältyy terveysriskejä, muuta tieteellisen kirjallisuuden perusteella kokonaisuutena kalan syöntiä voidaan pitää hyväksi ihmisen terveydelle. Tämä työ pyrkii tuomaan lisäymmärrystä niin kalan syöntiin liittyviin terveyskysymyksiin kuin arviointiin ja päätöksentekoon. Työ keskittyy kolmeen osa-alueeseen: 1) tieteellinen tieto 2) arviointimenetelmän valinta 3) taustatekijät ja arvostukset. Nämä kolme aluetta muodostavat päätöksenteon tuen.

Suomea voidaan Euroopan tasolla pitää paljon kalaa syövänä maana. Kala on omega-3 rasvahappojen tärkein lähde Suomessa joiden on useissa tutkimuksissa havaittu pienentävän verenkiertoelimistön sairauksien riskiä ja parantavan keskushermoston kehitystä lapsilla. Kaloista löytyvistä haitta-aineista kolme tärkeintä ovat metyylielohopea, dioksiinit ja PCB. Metyylielohopea rikastuu ravintoketjussa ylimpänä olevien eliöiden keskushermostoon. Etenkin lasten kehittyvä hermosto on altis metyylielohopean haitallisille vaikutuksille. Dioksiinit taas kerääntyvät rasvaan ja ovat kehossa hyvin pysyviä yhdisteitä. Itämeren rasvaisiin kaloihin, erityisesti silakkaan ja loheen, on kerääntynyt sekä dioksiinia että PCB:tä jonka takia nämä yhdisteet ovat olleet erityistarkkailussa Suomessa.

On tärkeää ymmärtää mitä kaikkia tekijöitä arviointiin tulee sisällyttää jotta se parhaiten toimisi päätöksenteon tukena. Ensiksikin, tarkoituksen ja tarpeen tulisivat olla arviointimenetelmän pääasiallisena valintaperustana. Viitearvoon perustuvissa arvioinneissa aiheen rajaus on tyypillisesti suppea, ja ne soveltuvat hyvin hallinnollisiin tarkoituksiin. Riskien arvioinnissa taas edetään askel pidemmälle arvioimalla altistumisen avulla terveysvaikutusten todennäköisyys. Vertailevassa riskien arvioinnissa useampia riskejä vertaillaan keskenään saaden kuvaa eri riskien mittasuhteista. Hyöty-riskiarvioinneissa taas pystytään tarkastelemaan yksittäisen aineosan sijaan koko ruoka-aineen terveysvaikutuksia. Hyötyjen arvioiminen onkin erityisesti kalan syönnin tapauksessa olennaista vaikka yleisesti hyötyjen ja riskien arviointiin sisältyy vertailua vääristäviä tekijöitä.

Myös eriluonteisten terveysvasteiden keskinäinen vertaaminen tuo lisähaastetta ja usein vertailussa päädytäänkin arvostuskysymyksiin. Tähän haasteeseen onkin pyritty kehittämään työkaluja. Mm. yhteismitallistavien (common currency) tekniikoiden avulla eri terveyden tiloja voidaan muuntaa yhteenlaskettavaan ja paremmin vertailtavaan muotoon. Tämä taas tarjoaa päätöksentekijälle mahdollisuuden vertailla monipuolisesti ja läpinäkyvästi eri vaihtoehtoja.

Objektiivisen tieteellisen tiedon lisäksi arviointien taustalla vaikuttaa monia intressejä joiden vaikutus päätöksen tekoon voi olla huomattava. Tässä työssä näitä

kutsutaan muiksi taustatekijöiksi. Nämä voivat olla yhteiskunnallisia tai yksilöllisiä arvostuksia tai valintoja. Yksilön tasolla nämä ilmenevät tavallisesti riskien kokemisina, henkilön emotionaalisina vasteina, joista pelko on näistä tyypillinen esimerkki ja hyvin vahva vaikutin riskien kokemisessa. On tärkeää ymmärtää, että taustatekijät ja riskien kokeminen vaikuttavat läpi koko arviointiprosessin ja että arvioinnin tarkoitus ja tarve määrittävät myös mitä taustatekijöitä arviointiin tulisi sisällyttää. Hallinnollisissa arvioinneissa taustatekijöiden vaikutus on tyypillisesti vähäinen kun taas osallistavissa arviointihankkeissa näiden osuus voi olla hyvin merkittävä.

Väitöskirjassa julkaistut osatyöt vahvistavat käsitystä kalan syönnin terveyshyödyistä ja ettei siitä ole merkittävää haittaa erityisryhmiä lukuun ottamatta. Virallisia kalansyöntisuosituksia noudattamalla voivat kansalaiset edistää terveyttänsä. Osatöissä kuitenkin havaittiin, että hyötyjen ja riskien jakautuminen ovat hyvin voimakkaasti sidottuja henkilön ikään ja siihen mitä kalalajeja syödään. Elohopean mahdolliset terveyshaitat aiheutuvat lähinnä sisävesikalojen syönnistä, kun taas dioksiinit kertyvät ihmiseen lähinnä villien kotimaisten merikalojen syönnistä.

Tällaiset seikat asettavat haasteita kalan syönnin terveysriskien ja -hyötyjen viestintään ja näihin tuleekin kiinnittää erityishuomiota. Myös lukuisten erilaisten arviointimenetelmien käyttö aiheuttaa haasteen selkeälle riskiviestinnälle, sillä jo arviointimenetelmän valinta voi ratkaista arvioinnin lopputuloksen. Työssä esitetty kolmijako (tieteellinen tieto, arviointimenetelmät, taustatekijät ja arvostukset) on arviointien lopputulosten ja päätöksenteon kannalta tehokas keino tarkastella kattavasti erilaisia päätöksenteon kannalta olennaisia tekijöitä.

Avainsanat: kalan syönti, terveys, riski, hyöty, arviointi, päätöksenteko

Contents

List of original papers

I Leino O, Tainio M, Tuomisto JT. 2008. Comparative risk analysis of dioxins in fish and fine particles from heavy-duty vehicles Author(s). RISK ANALYSIS Volume: 28 Issue: 1 Pages: 127-140

II Leino O, Karjalainen AK, Tuomisto JT. 2013a. Effects of docosahexaenoic acid and methylmercury on child's brain development due to prenatal fish consumption in Finland. Food Chem Toxicol. Apr;54:50-58

III Leino O, Kiviranta H, Karjalainen AK, Kronberg-Kippilä C, Sinkko H, Larsen EH, Virtanen S, Tuomisto JT. 2013b. Pollutant concentrations in placenta. Food Chem Toxicol. Apr;54:59-69

IV Karjalainen AK, Hallikainen A, Hirvonen T, Kiviranta H, Knip M, Kronberg-Kippilä C, Leino O, Simell O, Sinkko H, Tuomisto JT, Veijola R, Venäläinen ER, Virtanen SM. 2013. Estimated intake levels of methylmercury from fish in Finnish children. Food Chem Toxicol. Apr;54:70-77

V Pohjola MV, Leino O, Kollanus V, Tuomisto JT, Gunnlaugsdóttir H, Holm F, Kalogeras N, Luteijn JM, Magnússon SH, Odekerken G, Tijhuis MJ, Ueland Ø, White BC, Verhagen H. 2012. State of the art in benefit-risk analysis: environmental health. Food Chem Toxicol. Jan;50(1):40-55.

Abbreviations

AH = aryl hydrocarbon

ALA = alfa-linolenic acid

BMDL = benchmark dose lower confidence limit

BRA = benefit-risk Assessment

bw = body weight

CSF = cancer slope factor

CHD = coronary heart disease

CBA = cost benefit analysis

CEA = cost effectiveness analysis

DALY = disability adjusted life years

DHA = docosahexaenoic acid

EU = the European Union

EFSA = the European Food Safety Authority

EPA = eicosapentaenoic acid

EVIRA = the Finnish Food Safety Authority

FAO = the Food and Agriculture Organization

FDA = U S Food and Drug Administration

IARC =international agency for research on cancer

ICP-MS = inductively coupled argon plasma mass spectrometer

IQ = intelligence quotient

JECFA =the Joint WHO/FAO Expert Committee on Food Additives

LOQ = limit of quantification

MeHg = methylmercury

MMR = mild mental retardation

MCDM = multi-criteria decision making

NAS = the National Academy of Sciences

NDL-PCBs = non-dioxin-like PCBs

NOAEL = no-observed-adverse-effect level

NRC = national research council

NTP = national toxicology program

OTC = organotin compounds

PBB = polybrominated biphenyls

PBDE = polybrominated diphenyl ethers

PCB = polychlorinated biphenyls

PCDD = polychlorinated dibenzo-dioxins

PCDF = polychlorinated dibenzofurans

PCDD/F = polychlorinated dibenzo-p-dioxins and furans

PM2.5 = particulate matter, size fraction 2.5 micrometers

PCN = polychlorinated naphthalenes

POP = persistent organic pollutant

PTWI = provisional Tolerable Weekly Intake

QALY = quality adjusted life years

RfC = reference concentration

RfD = reference dose

RKTL = the Finnish Game and Fisheries Research Institute

SAB = scientific advisory board

SYKE = the Finnish Environment Institute

SCF = scientific committee on food

TCDD = 2,3,7,8- tetrachlorodibenzo-p-dioxin

TEQ = toxic Equivalence

TDI = tolerable Daily Intake

TBT = tributyltins

U.S.EPA = the U.S.Environmental Protection Agency

VSL = value of a statistical life

WHO = the World Health Organization

WTP = willingness to pay

VTT = technical Research Centre of Finland

1 Introduction and scope of the work

Research of human health effects due to fish consumption has been active for decades. The majority of the peer reviewed scientific publications suggest that benefits of fish consumption outweigh the risks (Mozaffarian and Rimm 2006; Park and Mozarrafian 2010; FAO/WHO 2011) but there are studies raising concerns both about contaminants in fish and their human health risks (e.g. Virtanen et al. 2007; Hites et al. 2004; Salonen et al. 1995; Karagas 2012). This dispute was also acknowledged by Bushkin-Bedient and Carpenter (2010). In addition to studying the health effects due to fish consumption, this thesis was inspired by a practical question:

Why different individual fish consumption related health risk assessments often produce different conclusions?

The main objective in this work is to analyze and discuss these factors and their contribution to societal decision making related to fish consumption. As a starting point and scoping the thesis, picture 1 presents the three main domains of the work; *research*, *societal needs*, and *other interests* (originally presented in Tijhuis et al. 2012b). Replacing the domain *societal needs* with a more specific subdomain, *assessment methods,* provide more emphasis on the assessment methodologies. Three domains presented in picture 1 (with a small clarification in form of changing *societal needs* to *assessment methods*) form the backbone of this work. First, the reasoning in this work is supported by quantitative health effect estimates acquired from the original publications included in this work, and from the scientific literature. Second, this work demonstrates the importance of choosing the assessment framework (called assessment method in this work). Third, this work suggests that decision making is also influenced by number of underlying factors and valuations.

Research domain deals with quantifiable measures, such as pollutant concentrations in fish, fish consumption estimations and toxicology of pollutants. Assessment methods domain focuses on the alternative ways of assessing health risks and benefits, scoping the assessment, and interpreting the results. A group of other dimensions, such as ethical, ecological, financial, and employment political factors are also important factors in the societal decision making. In this work they belong to “other interests” domain. The influence of these things on the assessment outcomes is often neglected, and therefore they were given a proper presentation in this thesis. Together the three domains presented in the picture 1 form the decision support. The domains also have an interplay, the center of the picture labeled 'shared understanding' in the picture by Tijhuis et al. (2012b), which reflects the situation where people agree on what facts and opinions there are about the issue. In the context of the thesis, this can be understood as a complex real life decision making situation in regulating fish consumption.

Picture 1. Scope of the thesis (Tijhuis et al. 2012b)

The scope of this work is on applying scientific information from fish consumption, assessments methodology, and other interests to form better understanding and decision support to the societal decision making.

2 Review of the literature

Literature review provides background information about the domains presented in picture 1, and it is divided into sections according to the domains. The first section contains information about the situation of fish consumption in Finland, and it presents the current understanding of the human health effects attributable to fish consumption. The second section presents various different means in assessing societal risks and how these assessment methods differ from each other. The third section deals with other interests. In the end of the thesis, general discussion synthesizes from both the literature review and from the original publications, and draws conclusions about risks and benefits of fish consumption.

2.1 Research

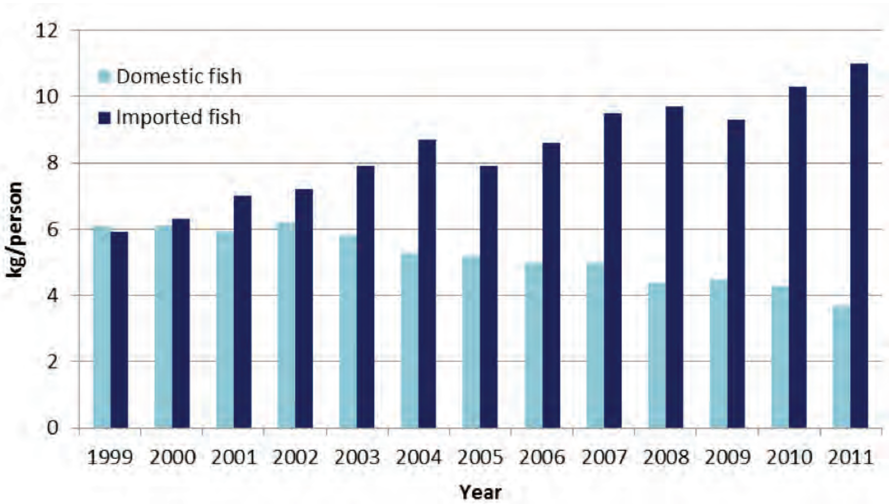
2.1.1 Description of the Finnish water areas

Finland is known as the land of thousand lakes. According to the Finnish Environment Institute (SYKE), there are 187888 lakes larger than 500 m2 in Finland. Most of the lakes were formed during the post glacial period when the glacier gradually pulled back to North. Generally, the lakes are very shallow. The average depth is only six meters, and the total volume of the lakes is 235 cubic kilometers (SYKE 2011). Furthermore, the ground is often both acidic and rich in organic matter, also swamps are very common. Because of these special features, Finnish freshwater areas are sensitive for accumulation of mercury (e.g. Munthe et al. 2007) which will be later described in detail.

The Baltic Sea has been recognized as an environmentally problematic area due to high concentrations of persistent organic pollutants (POP) in marine life. It is a shallow inland sea and the only link to the Atlantic Ocean is through a narrow sound in Denmark, making it vulnerable for contaminants to accumulate in the sea. SYKE surveys nutrient concentrations in Finland as nutrient load to the Baltic Sea is also a concern. However, in this work only chemical pollutants are covered.

2.1.2 Fish consumption in Finland

Finns are one of the top consumers of fish in Europe. The average annual fish consumption in Finland is 35 kg/capita (fresh weight) (Aquamedia 2010). For comparison, the leading countries in the European Union (EU) are Portugal (58 kg/capita), and Spain (38 kg/capita). The EU average is approximately 24 kg/capita, while the world average was recently around 13 kg/capita per year (Aquamedia 2010.) This warrants Finland to be called a high fish consumption country, and therefore studying the fish consumption mediated health effects is of great importance. According to the recent study by the Finnish Game and Fisheries Research Institute (RKTL), Finns consume 3.8 kg domestic fish (in filleted weight), and 11.5 kg imported fish (in product weight) (RKTL 2012). The amount of the total fish consumption has been stable for the last decade but there is a clear decreasing trend in domestic fish consumption and an increased trend in imported fish consumption (picture 2) (RKTL 2010). Because of this trend, the number of Finnish fishermen has been decreasing steadily during the last decade (RKTL 2012; Turunen 2012). Tables 1 and 2 present domestic and imported species specific fish consumption, respectively (RKTL 2012). Consequently, it can be seen that the recreational fishery dominates the domestic fish consumption (table 1), but it is still only 15% of the amount of imported fish consumption.



Picture 2. Fish consumption in Finland 1999-2011 (RKTL 2012).

Table 1. Consumption of domestic fish in Finland in kg per person as filleted weight, by origin in 2011 (RKTL 2012). Numbers 0.0 refer that the number is smaller than the significant figures shown.

Species	Commercial fishery	Recreational fishery	Aqua-culture	Total
Rainbow trout	0.0	0.0	0.9	0.9
Vendace	0.4	0.2	0.0	0.6
Pike	0.0	0.6	0.0	0.6
Perch	0.1	0.4	0.0	0.5
Baltic herring	0.3	0.0	0.0	0.3
European whitefish	0.1	0.1	0.1	0.3
Pikeperch	0.1	0.2	0.0	0.3
Other	0.1	0.2	0.0	0.3
Total	1.0	1.7	1.1	3.8

Table 2. Consumption of imported fish in Finland in kg per person as product weight in 2011. (RKTL 2012)

Species	Product weight
Salmon	4.1
Tuna (canned)	1.7
Rainbow trout	0.9
Shrimp	0.7
Saithe (filleted frozen)	0.6
Herring (preserves)	0.4
Other	3.1
Total	11.5

2.1.3 Chemical contaminants in Finnish waters

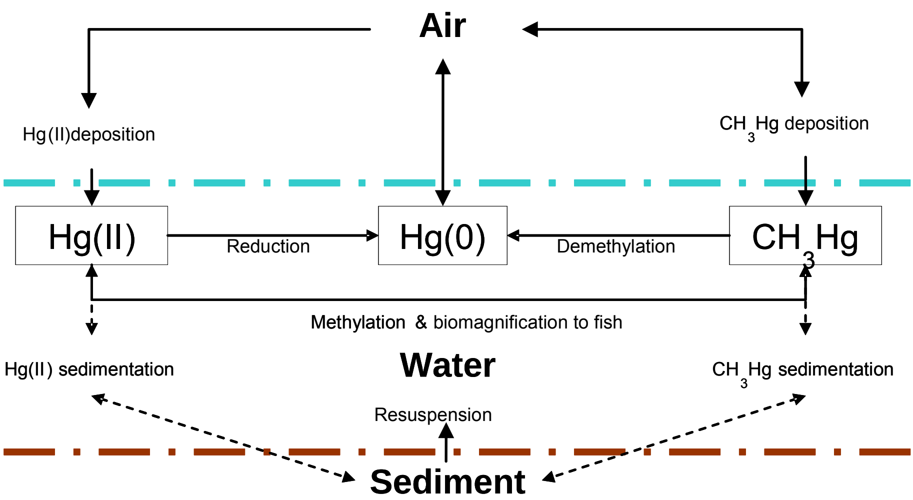
The sources and nature of chemical contaminants are very different, and also marine and freshwater areas have distinctive features. First, acidic conditions of soil typical in inland areas promote the methylation process of mercury (picture 3) to form methylmercury (MeHg) which easily enters the food chain. Therefore, MeHg concentrations in fish are usually slightly higher in freshwater areas (Hallikainen et al. 2004). Second, countries surrounding the Baltic Sea practice intensive forest industry, where wood protection agents containing polychlorinated dibenzo-p-dioxins (PCDD/Fs) as impurities were under intensive use. Third, PCDD/Fs are also formed in by-processes of incineration where burning temperatures are not high enough. Fourth, PCBs were widely used in various industrial and technical applications which caused them to bioaccumulate in food chain to animals and they are removed from the food web very slowly.

Although dioxins are not purposely manufactured and used, there are significant historical point sources of dioxin from old forest industry plants (Isosaari et al 2002; Verta et al 2007), and these have been responsible for some of the regional dioxin hot spots. However, studies also indicate that in general atmospheric deposition is currently the most important ambient source of dioxins (SEPA 2009). A modeling study (Gusev 2009) suggests that the net annual deposition of dioxins to the Baltic Sea decreased about 60% from 1990 to 2007.

This work takes into consideration 1) contaminants where fish is the major source of exposure, and 2) where there is good evidence of human toxicity. Three contaminants fall into this category in Finland; MeHg, dioxins, and PCBs. Additionally, contaminants with lesser evidence on the human toxicity, but whose exposure comes mainly from fish, are also briefly introduced.

2.1.3.1 MeHg

Mercury in the environment can be found in different chemical forms. Sediment is the source of elemental mercury which can be transformed to other forms in different physiochemical conditions. In most foodstuffs mercury appears predominantly in its inorganic forms but in fish, most of the mercury is found in the more toxic, organic, form. Organic mercury, namely methylmercury (MeHg), accumulates in the aquatic food webs into predatory fish species, such as pike and pike-perch, whereas inorganic mercury progressively declines in food webs (Björnberg et al. 2005). Therefore, humans are primarily exposed to MeHg via their diet, mainly from fish consumption. In Finland, total MeHg exposure almost exclusively comes from fish consumption (Hallikainen et al. 2010). Also globally, air and water exposure pathways are considered to contribute little to the daily intake of MeHg (Freire et al. 2010). Picture 3 presents a simplified illustration of mercury cycle across air, water and sediment surfaces.



Picture 3. Mercury cycle in the aquatic environment. CH3Hg stands for methylmercury, Hg (II) and Hg (0) for forms of elemental mercury (adapted from USGS 2013).

For elemental mercury vapor, the most important source for the general population is dental amalgam. However, occupational exposure may exceed this by many times. Evaporation of elemental mercury from dental amalgams is suggested to be a less significant health risk compared to other types of mercury exposure (UNEP 1998). Actually, the removal of amalgams might cause a high short-term exposure if the operation is not dealt with extra care (Mercury 2011).

The main anthropogenic sources of mercury are the combustion of fossil fuels, smelting of metal, production of cement, and waste incineration. Direct aqueous releases from paper industry and related mercury-based chlor-alkali production caused elevated MeHg concentrations in both lakes and coastal waters in Finland (UNEP 1998). Fortunately, the abandonment of the use of mercury compounds for slimicides in paper production in 1968, and decreasing demand for chlorine significantly reduced the releases of mercury. However, mainly due to the naturally high mercury levels in the Finnish soil, the mercury concentration limit of 0.5 mg/kg in fish, recommended by the World Health Organization/Food and Agriculture Organization (WHO/FAO), were exceeded among one kilogram pikes in 85% of the lakes in southern and central Finland in the end of the last century (Verta 1990).

Soil weathering processes and volcanic eruptions form the natural background. MeHg concentration in acuatic environment depends on factors such as pH and redox potential of the water, and species, age and size of the fish (UNEP 1998). Airborne mercury, mostly in the elemental form, can be transported over long distances. It is deposited in rain and then enters aquatic ecosystems. Most of the total mercury in fish is present in the form of MeHg (Kannan et al. 1998, Downs et al. 1998).

Mercury is toxic in all of its forms, but MeHg poses the biggest threat to human health due to its significant biomagnification potential and high toxicity. MeHg binds to proteins and is thus distributed into edible parts of the fish. Moreover, it is readily absorbed and distributed throughout the human body, and it easily crosses both placenta and blood-brain barrier and accumulates in the foetus brain (Diéz et al. 2008). Luckily, the general population does not face a significant health risk from even relatively high environmental MeHg exposure. However, there is both clinical and epidemiological evidence indicating that during gestation the organism is much more sensitive to the toxic effects of MeHg. Additionally, because there is a high requirement for the protein synthesis in foetal brain, the nervous system and foetal brain are the principal target tissues for the health effects of MeHg (UNEP 1998; WHO 1990). For these reasons, pregnant women and young children are considered as the special risk groups for MeHg exposure.

MeHg has also been suggested to be linked to cardiovascular endpoints, such as coronary heart disease (CHD), myocardial infarction, atherosclerosis, and acute myocardial infarction (Virtanen et al. 2007; Roman et al. 2011; Salonen et al. 2000; Salonen et al. 1995; Karagas 2012). Later on, Virtanen et al. (2012) stated that MeHg may reduce the beneficial effect of omega-3 fatty acids. However, FAO/WHO (2011) concluded that there is absence of probable or convincing evidence on risk of CHD associated with MeHg. Moreover, a large study conducted by Mozaffarian et al. (2011) was not able to show the association between mercury exposure and cardiovascular diseases. In fact, higher MeHg concentrations were associated with lower risks for cardiovascular effects, probably thanks to other beneficial substances found in fish. Similarly, the WHO published a report where, in addition to cognitive effects, they considered also other adverse health endpoints of MeHg but concluded that there is not enough evidence to support the association between MeHg and cardiovascular, skin, renal or neurophysiological symptoms (Poulin and Gibb 2008).

Biomarkers are often used in assessing health responses in humans. Hair can be used as a marker of MeHg exposure. Studies conducted after the mass outbreak of MeHg poisoning in Iraq claimed that maternal hair mercury concentrations as low as 10-20 µg/g during pregnancy were associated with a 5% risk of first MeHg-evoked symptoms in their offspring. McElhatton (2000) estimated that hair mercury concentration of more than double (50 µg/g) poses an equivalent risk for the adults. In comparison, maternal hair mercury concentrations in Finland are generally more than 20-times lower than in the Iraq mass outbreak. Additionally, a report by Vahter et al. (2000) found higher mercury concentrations in umbilical cord blood than the mercury concentration in the blood of the pregnant mother which further supports the finding that prenatal period is a highly susceptible time for mercury poisoning. MeHg -evoked severe developmental and behavioral deficits in the offspring can appear without any symptoms of Hg poisoning in the mother during pregnancy. There are a number of studies on MeHg on human health, and two major epidemiological studies on MeHg evoked human health effects: 1) the Faroe Island birth cohort study (Grandjean et al. 1997) and 2) the Seychilles child development study (Davidson et al. 1998). Most of the current knowledge, including several reviews (Cohen et al. 2005b, Axelrad et al. 2007) draw from these studies. These two epidemiological studies have been under a critical review, and they are considered to be the best sources of information on MeHg and adverse human health effects. Interestingly, there were differences in the conclusions of the two studies because they provide slightly different views on the potential health effects of MeHg. The factors possibly causing biases and uncertainties refer to exposure, selection of neurobehavioral endpoints, confounders, statistics, and study design. National Toxicology Program scrutinized the two major studies and examined their possible differences (NTP 1998). They concluded that there were no fatal flaws in either the Faroes or Seychelles studies, and both studies are commendable in terms of design, analytic strategy, and consideration of a wide range of confounders. However, the group acknowledged number of potential sources of uncertainty and bias, such as selection bias, effects of culture and language, influence of age, different order how tests were administered, and nutritional factors (especially PCBs, omega-3 fatty acids and selenium). The National Academy of Sciences (NAS) panel also reviewed the Faroes and Seychelles studies using additional data from a smaller New Zealand study (Crump et al. 1998), and found that additional data supports findings of the Faroe study, the association between MeHg exposure and adverse outcomes (Jacobson 2001). More recent cohort studies have examined the relationship of prenatal fish consumption, and have generally showed either no adverse effects or improved neurodevelopment among children whose mothers consumed more fish in pregnancy (e.g. Budtz-Jørgensen et al. 2007; Gale et al. 2008; Hibbeln et al. 2007)

A potential way of evaluating the variety of MeHg mediated symptoms in nervous system (such as impaired memory function, language skills, and attention deficits) is to use Intelligent Quotient (IQ) as a common metric. It combines neurological effects into one measurable unit, IQ points. IQ is currently considered as the best available marker of overall central nervous system status because it can broadly capture different cognitive effects. Though using IQ is practical, it also comes with limitations. IQ has been regularly misused or misunderstood, especially when applied to compare intelligence of individuals. Rather, it should be used for population level analyses. For example, a small decrease in IQ (a point or two) caused by MeHg exposure might be of a very minor concern for an individual but at the population level the impact might be a major public health concern (Rice et al. 2010).

The beneficial effect of selenium has been debated during the last decade. Choi et al. (2008) found no evidence that selenium provides an important protective factor against MeHg neurotoxicity, and selenium intake is not able to explain the benefits associated with fish intake. Nevertheless, research in this field is active. In 2007, Ralston found that Hg toxicity was more directly related to the mercury to selenium ratios (Heath et al. 2010; Mercury 2006; and Ralston 2009).Therefore Ralston and Raymond (2010) stressed the need for examination of this ratio in freshwater fish.

Regulations on MeHg

Intake of MeHg is regulated by several institutions. The two best established limit values have been provided by the U.S. Environmental Protection Agency (U.S.EPA) and the WHO. In 1995, U.S.EPA derived reference dose (RfD) 0.1 µg per kilogram of bodyweight per day (µg/kg bw/d) for MeHg. In terms of blood concentration, the total blood mercury concentration for women of childbearing age should stay lower than 5.8 µg/l (Schober et al. 2003). The Joint WHO/FAO Expert Committee on Food Additives (JECFA) set the level more than double the reference value of the U.S.EPA RfD. This is called Provisional Tolerable Weekly Intake (PTWI) and it corresponds to MeHg intake of 0.23 µg/kg bw/d. Maternal MeHg exposures from fish in Finland typically range from 0.03 to 0.06 µg/kg bw/d (Leino et al. 2013a), well below the limit values proposed by the U.S.EPA and JECFA.

As an example how guidance values (noncancer health end point) can be deduced, table 3 presents an approach proposed by the Health Canada, used for defining fish consumption recommendation (Mergler et al. 2004). As a starting point, they use MeHg concentration of mother's hair as biomarker of human exposure. Next step is to calculate on what MeHg exposure rate would mother have to have in order to achieve the hair mercury concentration with the first adverse effects seen in offspring. Adopting safety factor tries to take into account individual variability. Apart from the other steps relying on toxicology or quantifiable measures, applying safety factor is mainly a tool of risk management. After this, Tolerable Daily Intake (TDI) can be calculated and finally, number of fish meals per time period can be calculated based on the average bw of the population (e.g. 60 kg) and fish portion size (e.g. 230 g).

Table 3. Process of determining fish consumption recommendation due to MeHg exposure.

Step	Value adopted by the WHO
1. Determination of exposure threshold	14 ppm in the hair
2. Calculation of daily intake	1.5 µg Hg/kg/d
3. Application of a safety factor	Safety factor 6.4 (from 4.5 to 10, depending on the institution)
4. Calculation of tolerable daily intake (TDI)	0.23 µg Hg/kg/d
5. Calculation of number of meals per month	e.g. twice a week. Depending on local mercury levels in fish, body weight and typical portions of fish consumed

Generally, the WHO RfD is not exceeded by the majority of the population but the safety of avid fish consumers, particularly the safety of their children, is a concern. Currently, National Food Safety Authority of Finland (EVIRA) advises pregnant women to eat a variety of fish at least two times per week. Additions to the general recommendation are 1) herring larger than 17 cm in length or salmon from the Baltic Sea only 1-2 times per month, 2) pike only 1-2 times per month, 3) people who consume freshwater fish on a daily basis, should avoid eating large pike-perch, perch and burbot, 4) pregnant women should avoid eating pike. Table 4 shows a variety of limit values available, set by different institutions. The first four limit values refer to intake of MeHg, and can be considered the most accurate sources of information. Again, the 2.3 times difference between the U.S.EPA and JECFA values can be seen as a signal of uncertainty in the proposed limit values. The first four limit values require detailed information on MeHg concentration in food stuff and precise weights. However, they might not be practical pieces of consumer information, rather general fish consumption recommendation and maximum concentrations in fish often provide more useful information for the consumers.

Table 4. Limit values of MeHg exposure set by different institutions.

Limit value	Organization	Value
Reference dose (RfD)	U.S.EPA[a]	0.1 µg/kg bw /day
Provisional tolerable weekly intake (PTWI)	JECFA[b] FAO/WHO	1.6 µg/kg bw /week
Tolerable daily intake (TDI)	WHO[c]	0.23 µg kg bw/day Hg
Tolerable daily intake (TDI)	Health Canada[d]	0.20 µg /kg bw/d (unborn child)
Maximum MeHg concentration in fish for sale	Ministry of Trade and Industry, Finland[e]	0.5 mg/kg
MeHg concentration in animals	JECFA. Environmental Quality Standards for animals[b]	0.002 – 1 ng/g freshweight
MeHg concentration in water	EC, Environmental Quality Standards for water[f]	0.047 µg/l total dissolved Hg
General fish consumption recommendation in Finland	EVIRA[g]	Two times per week, mixing various species in diet.

[a] U.S. Environmental Pollutant Agency

[b] (JECFA)

[c] World Health Organization (WHO)

[d] Mergler et al. 2004

[e] Mäntynen 2007

[f] European Commission 2005

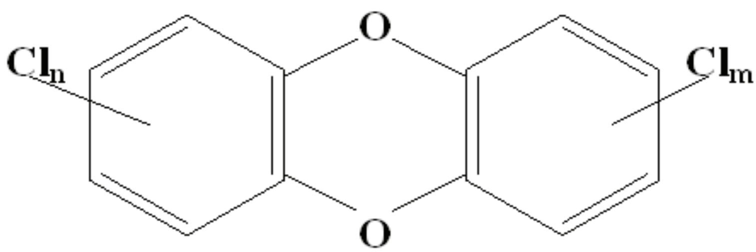
[g] Food Safety Authority, Finland (EVIRA)

2.1.3.2 PCDD/Fs

PCDD/Fs, generally referred as "dioxins", have been labeled as the most toxic man-made chemicals. The primary health concern used to be carcinogenicity. From the public health point of view, concern about cancer is justified; 50% of males and 33% of females in Sweden develop cancer during their lifetime (Sytyke 2013). However, other PCDD/F health risks, such as developmental and reproductional disorders, immune function, and diabetes, are currently considered as potential and topical health risk end points (The National Academies Press, 2006).

Dioxins belong to groups of polychlorinated dibenzo-p-dioxins (PCDD) (picture 4) or polychlorinated dibenzofurans (PCDF). Congeners that have chlorines in positions 2, 3, 7, and 8 possess "dioxin-like" properties. The term dioxins is very often used to refer to sum of compounds (seven congeners of dioxins, ten furans and twelve PCBs). In 1990, WHO established TDI of 10 pg/kg bw for TCDD (WHO 1998). The toxicity of PCDD/F is mediated through the aryl hydrocarbon (AH) receptor. Binding to the AH receptor induces many genes, including cytochrome P450 1A1 enzyme which function to break down toxic compounds (Pohjanvirta 2009).

Studying the combined effects of different carcinogens is very complex. Also dioxin congeners vary greatly in toxicity and therefore the concept of toxic equivalence (TEQ) has been developed. This enables to sum up the toxicity of the whole group, and it has been used extensively in assessing both exposure and adverse health effects. They key concept in TEQ approach is called Toxic Equivalence Factor (TEF). For each dioxin congener, there is an assigned relative toxicity compared to the most potent dioxin congener 2,3,7,8- tetrachlorodibenzo-p-dioxin (TCDD), and the TEF values vary from 1 to 0.00003. Various sets of TEF values have been developed, e.g. WHO-TEF, Nordic TEF and international TEF or I-TEF but WHO-TEF approach is the most commonly used. The latest re-evaluation of TEF values was conducted by WHO in 2005. (Tuomisto et al. 2011)



Picture 4. General chemical structure of PCDDs.

Dioxins are by-products of industrial processes. They remain in a stable form once released in the environment. Emissions have decreased during the last decades (EFSA 2005; Tuomisto et al. 2011). They are metabolized and excreted very slowly. Half life is commonly used for describing how persistend substances are. Dioxins are lipophils and they bioaccumulate and become biomagnified in animals, and therefore dioxin congeners have long half-lives in humans, up to decades. This makes them different to MeHg which have much shorter half live, 72 days in aquatic systems (U.S.EPA 2001). Half life also relates to the lag in decline of concentrations in the environment. This means that dioxins persist in the environment much longer, which is also seen in the Baltic Sea. After controlling dioxin emissions there was a clear decline in the concentrations, but recently the decline has gradually leveled off (Hallikainen et al. 2011). Therefore, fish is still the biggest source of human exposure to dioxin in Finland, approximately 95% of dioxin exposure originates from fish (Kiviranta et al. 2004).

Since environmental concentrations are typically low, epidemiological evidence for dioxin almost exclusively comes from contamination incidents. The best-known dioxin accident took place in 1976 in Seveso, Italy, where a trichlorophenol production reactor in a chemical factory blew up and released kilogram quantities of TCDD to the environment. Chloracne was observed in about 200 persons but no other direct adverse health outcomes were noted. Individual variation was also remarkable, some individuals developed symptoms when their exposere was 1000 pg/g (in lipid) whereas some individuals were free from symptoms after exposed to more than ten times higher concentrations (Sytyke 2013). After 25 year follow-up, there was no health difference between the exposed and controls, including mortality and cancer incidence. However, changes in tooth development and decreased male offspring of persons exposed as small children were noted.

Several dioxin accidents of smaller scale have taken place, such as citrus pulp pellet incident in 1997 in Brazil, animal feed contamination incident in 2010 in Germany, hazardous waste site incident in 1979 in New York, and salvage oil incident in 1971 in Eastern Missouri (Tuomisto et al. 2011).

Regulations on PCDD/F

Table 5 shows diversity of dioxin guidance values in terms of concentration of dioxin in foodstuff and feed. The concentrations in the Baltic herring, the most dioxin-contaminated fish species in the Baltic Sea, typically range from 4 to 10 pg/g in fresh weight, and 20-30 pg/g in fat (Hallikainen et al. 2004). Finland and Sweden have been previously granted a derogation from the EU for selling fish exceeding the maximum concentrations of dioxins and PCBs (EY 1259/2011). In 2011 the derogation became permanent. The reason for the derogation is the evidence of large health benefits acquired from fish consumption. Table 6 presents TDI values per day, figures include dioxins and dioxin-like PCBs. There is a time trend moving into strickter TDIs. The TDIs in the table also fall pretty close together, only WHO 1990 is clearly higher than the other TDIs. Average population total intake of PCDD/F in 2005 in Finland was 54 pg/d WHO TEQ and respective intake of PCDD/F + dioxin-like PCBs 114 pg/d (WHO TEQ), which are under the maximal recommended intakes (Hallikainen et al. 2010). In 2005, the average intake of young women in Finland was estimated at 1.5 pg/kg bw/d (Kiviranta et al. 2005).

Table 5. Guidance values for dioxin concentration in foodstuff and in fish in the EU

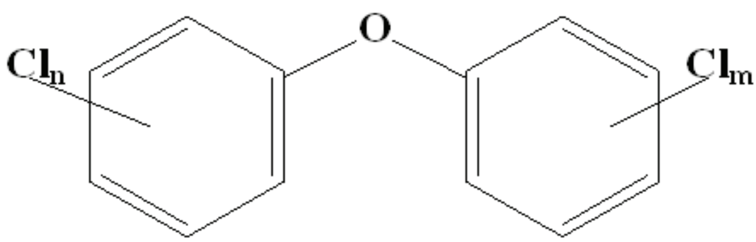
Limit value	Value
Food fish (EY 1259/2011)	3.5 pg/g fresh weight
Food fish (including dioxin-like PCBs) (EY 1259/2011)	6.5 pg/g
Meat and meat products (EY 1259/2011)	1-2.5 pg/g fat (WHO-PCDD/F-TEQ)
Milk products (EY 1259/2011)	2.5 pg g/fat (WHO-PCDD/F-TEQ)
Hen eggs and egg products (EY 1259/2011)	2.5 pg/g fat (WHO-PCDD/F-TEQ)
Oils and fats (EY 1259/2011)	0.75 pg/g fat (WHO-PCDD/F-TEQ)
Feed: Fish, other aquatic animals, their products and by-products with the exception of fish oil (IP 2002)	1.25 ng/kg (WHO-PCDD/F-TEQ)
Feed: Fish oil (IP 2002)	6 ng/kg (WHO-PCDD/F-TEQ)

Table 6. Maximal daily intakes of PCDD/F (WHO TEQ PCDD/F-PCB). (U.S.EPA 2009; European Commission 2000)

Organization	Value (pg/kg bw/d)
JECFA (2001)	2.3
WHO (1990)	10
WHO (1998)	1-4
Japan (1998)	4
Nordic countries (2000)	5
United Kingdom (2001)	2
Scientific Committee on Food (SCF)	2

2.1.3.3 PCBs

PCBs consist of 209 organic compounds where up to ten chlorines are attached to two benzene rings (picture 5). Because PCBs are structu rally similar to dioxins and furans, especially so called dioxin-like PCBs that bind the AH receptor, they share many same features with PCDD/Fs, and the toxic effects produced by PCBs are similar to PCDD/Fs. Moreover, PCBs do not readily degrade in the human body or in the environment. TEQ approach is also used with dioxin-like PCBs by comparing PCB congener toxicity to TCDD using TEFs. This way combined effects of all PCB congeners can be relatively easily taken into account. The methodology, set by the WHO, and the resulting overall concentrations are referred to as WHO-TEQs, analogous with dioxin (WHO 1998). The latest re-evaluation of TEF values was conducted by WHO in 2005 (Tuomisto et al. 2011).



Picture 5. General chemical structure of polychlorinated biphenyls

PCBs have been widely used in several industrial purposes, such as coolants and insulation fluids, in paints and cements, electrical wiring and sealants. PCB production was banned in the United States in 1979 (United States Congress), and globally in 2001 (Stockholm Convention on Persistent Organic Pollutants). Burning PCBs also poses a risk of generating dibenzo-p-dioxins and dibenzofurans in incomplete combustion.

Despite the banning of PCBs in 2001, 80% of PCB exposure in Finland comes from fish consumption (Kiviranta et al. 2004). Emissions have been declining (Kiviranta et al. 2004) but fatty fish species, such as salmon and herring in the Baltic Sea, frequently exceed the maximum concentration given for dioxins and PCBs (Hallikainen et al. 2011). Concentrations of dioxins and PCBs are typically much lower in freshwater fish than in fish from the Baltic Sea (Hallikainen et al. 2010).

Epidemiological studies have reported that PCBs pose adverse effects on neurological performance and cognitive development in children 6–11 years of age (Aoki 2001; Boersma and Lanting 2000; Chen et al. 1992; Jacobson and Jacobson 1996; Stewart et al. 2008; Vreugdenhil et al. 2002). Other possible human health effects with less evidence include liver damage, dermal and ocular lesions, irregular menstrual cycles, reduced immune reactions, fatigue, unusual skin sores. Due to lack of human data, the lowest exposure levels associated with human health effects are usually not established. PCBs are also suggested to be associated with cancer (classified as probable human carcinogens by the WHO, National Cancer Institute, IARC, and EPA). National Toxicology Program (NTP) has confirmed PCB126 and a binary mixture of PCB126 and PCB153 (Technical Report 531). The evidence and dose-response data is, however, insufficient for quantitatively assessing PCB risks, therefore dioxin-like PCBs are generally considered to contribute to the same health endpoints with dioxins. Similar to dioxins, PCBs are also currently considered as cancer promotors, rather than initiators. Maximal tolerable daily intake of PCB is 2 pg WHO TEQ/kg bw. This figure includes also intake of PCDD/Fs. The estimated intake of PCBs in Finland is 60 pg WHO TEQ/d (Hallikainen et al. 2010), well below the TDI (for 70kg person 140 pg WHO TEQ/d).

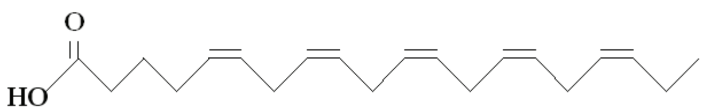
Because PCBs are not released into the environment on purpose, epidemiological data is acquired from different accidental releases of PCB. Incidents have taken place all over the world, for example in Ireland 2008, Italy 2001, Belgium 1999, Slovakia 1984, Taiwan 1979, UK 1970s, Japan 1968 and several incidents in the U.S.

In addition to the 12 PCB congeners possessing dioxin-like properties the rest of the PCB congeners are referred to as non-dioxin-like PCBs (NDL-PCBs). They have non-planar structure and have a complex spectrum of adverse effects, but lack a detailed risk assessment (Stenberg et al. 2011). Sum of the six indicator non-dioxin-like PCBs were five times higher than the sum of the 12 dioxin-like PCBs, and these high concentrations are the reason for scrutinizing the health effects of the non-dioxin-like PCBs. Some of the NDL-PCBs are known to elicit neurological, endocrine, immunological and carcinogenic effects (EFSA 2010b). A novel mode of action in toxicity of NDL-PCBs was found by Langeveld et al. (2012). ATHON (Assessing the Toxicity and Hazard of Non-dioxin-like PCBs Present in Food) project was conducted to provide health hazard information, and to clarify biological mechanisms underlying toxicity of NDL-PCBs. However, further studies are needed to characterize the risk of NDL-PCBs.

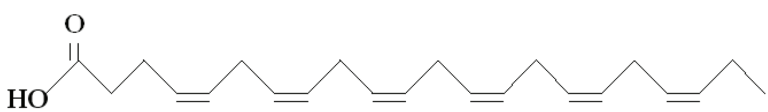
The regulation of dioxin-like PCBs is often presented together with PCDD/F because of the similar toxicological mechanisms (for example in table 6). Due to lack of understanding, regulation for NDL-PCBs is still work in progress.

2.1.3.4 Omega-3 fatty acids

Omega-3 fatty acids stand for a family of polyunsaturated fatty acids. They have carbon–carbon double bond in the third bond from the methyl end of the fatty acid. The group includes alfa-linolenic acid (ALA), eicosapentaenoic acid (EPA) (picture 6), and docosahexaenoic acid (DHA) (picture 7) which are the main compounds manifesting beneficial health effects of fish consumption Generally, DHA appears important for early neurodevelopment and EPA for cardiovascular endpoints.



Picture 6. Chemical structure of EPA.



Picture 7. Chemical structure of DHA.

Intake of omega-3 fatty acids mainly comes from fish consumption and EPA and DHA are acquired almost exclusively from the diet, namely from marine animals. Further, our body is capable of producing very limited amounts of EPA and DHA from ALA, only 5-10% of the dietary ALA can be converted into EPA, and 2-5% of

EPA can be further converted into DHA (Goyens et al. 2005; He 2009; Jones and Kubow 2006). This makes direct intake of EPA and DHA vital.

Beneficial effects of EPA on heart health and circulation have been studied extensively for a period of time already, and association of fish consumption and decreased mortality is supported by several meta-analyses (e.g. He et al. 2004; Whelton et al. 2004; Zheng et al. 2011) and systematic reviews (Wang et al. 2006; von Schacky 2007). Intake of EPA may also reduce the risk of secondary and primary heart attack (Bucher et al. 2002), stroke (Delgado-Lista et al. 2012), and CHD (König et al. 2005). It also reduces blood diglyseride levels (Harris 1997; Davidson et al. 2007). Despite the WHO statement about lack of evidence in MeHg induced cardio vascular health effects (Poulin & Gibb 2008), some studies suggest that MeHg exposure may reduce, but not negate, the cardiac health benefits of omega-3 fatty acid intake (Mozaffarian and Rimm 2006; Virtanen et al. 2012; Stern 2005).

There is also good evidence of beneficial effects of DHA intake on central nervous system. These effects include treatment of variety of mental disorders, including bipolar disorder, attention deficit hyperactivity disorder, depression, dementia and developmental disorders (Perica & Delas 2011; Montgomery & Richardson 2008; Naliwaiko et al. 2004; Mazereeuw et al. 2012; Richardson & Montgomery 2005, respectively). A potential metric for evaluating the various different effects on central nervous system is IQ, which aggregates several different neurological effects into one measurable unit. IQ was already introduced as a marker of adverse effects of MeHg exposure (page 25). Despite the probable positive associations, the epidemiological evidence can still be considered challenged, including all cause mortality (Rizos et al. 2012), myocardial infarction (Kwak et al. 2012) and coronary events (Kotwal et al. 2012).

The therapeutical range of DHA on a health endpoint varies a lot depending on endpoint, from tens of milligrams to several grams per day. The European Food Safety Authority (EFSA) has given recommendation for sufficient intake of EPA and DHA on several health endpoints, such as cognitive function, brain development, eye health, heart health, nerve development, maternal health, skin and digestive tract, mood, blood health, and anti-inflammatory action (EFSA 2011). Although empirical evidence is still lacking, guidelines recommend DHA intake of approximately 100–300 mg/day during pregnancy (Akabas and Deckelbaum 2006; Koletzko et al. 2007). Also American Heart Association (AHA) has given a recommendation that those diagnosed with CHD should consume EPA/DHA at least 1 g/day from oily fish or supplements in order to decrease risk for heart diseases, and persons in need of lowering blood triglycerides should consume 2–4 g of EPA and DHA per day in the form of supplements (Kris-Etherton et al. 2002). Further, FDA has advised that adults can safely consume a total of 3 grams per day of combined DHA and EPA (Bent et al. 2009: Koletzko et al. 2007). Mozaffarian and Rimm (2006) published a large study where health endpoints of omega-3 fatty acid intake are presented. The relative strength of evidence was found to be best in antiarrhythmic endpoint, which is typically achieved already at dietary doses. Antithrombotic effect intake level is typically met on supplemental doses. Further, 250 mg/d of EPA and DHA was estimated to be a reasonable target intake to reduce CHD mortality.

Turunen and coworkers (2012) have published series of publications studying the relationship between the fish consumption and the population health data in Finland. They selected a high fish consumer group, fishermen and their spouses, and compared health events in this population subgroup with the general population. The main finding was that fishermen and their wives had lower all cause mortality than in the general population (Turunen et al. 2008). Additionally, they concluded that high intakes of environmental contaminants in fish were not seen as excess mortality to e.g. cancer or other causes linked to the contaminants. In Turunen et al. (2008), the group also suggested that environmental contaminants are slightly better biomarkers of fish consumption than omega-3 fatty acids in the Baltic Sea area. Further, Turunen et al. (2011) found that fish consumption is associated with consumption of other healthy food, such as vegetables, fruit and berries, and they have to be considered as confounders in dietary assessments studying the effects of fish consumption. This implies that population generally acknowledge fish as part of a healthy diet.

2.1.3.5 Other environmental pollutants and nutrients found in fish

There are several other substances in fish potentially harmful or beneficial for human health. Only substances where fish is considered to be a significant source of human exposure in Finland are briefly introduced.

Polybrominated diphenyl ethers

Polybrominated diphenyl ethers (PBDE) are used as flame retardants e.g. in electronics, furnitures, airplanes, and plastics. There are a total of 209 PBDE substances, and they bioaccumulate into blood, breast milk, and fat tissues. Their similarities with PCDD/F and PCB stimulated the need to study their potential to cause adverse human health effects. Moreover, they are used in a wide variety of consumer products, including furniture, electronic, and household products, as flame retardants. Humans are primarily exposed to PBDE via diet. In Finland, the total intake estimation is 43 ng/d, and fish consumption contributes 55% of the total intake (EVIRA 2009). PBDEs have been suggested to pose risk for liver toxicity, thyroid toxicity, endocrine-disrupting activity and neurodevelopmental toxicity (Main et al. 2007; U.S.EPA 2008; EVIRA 2009). The EU has completely banned the use of the so called penta-mixtures since 2004 (European Commission 2003), and the manufacture of the most potent PBDE congeners have been banned or restricted in several countries. There is no evidence on the human toxicity with the current intake levels of PBDE in the environment. However, this group of pollutants needs further studying (EVIRA 2009).

Polybrominated biphenyls

Similar to PBDEs, PBBs are also used as flame retardants. They can be found in e.g. plastics products, home electrical appliances, and textiles. Structurally polybrominated biphenyls (PBB) are alarmingly similar to dioxins and PCBs, the only difference to PCB is the bromine atoms attached in PBDE, instead of chlorine. PBBs were banned in the U.S. after Michigan incident in 1973, where PBBs accidentally entered the food chain and contaminated dairy products. After this, PBBs were replaced by PBDEs which have been widely used in the U.S. since the 1970s. The clearest evidence for their health effects is their property to cause skin problems, such as acne (McDonald 2002). Evidence for carcinogenicity is weak, and IARC has classified PBB as possibly carcinogenic for humans whereas U.S.EPA has not classified PBBs to be carcinogenic (IARC 2007; U.S.EPA 2008). PBBs were listed as one of six controlled substances under the Restriction of Hazardous Substances Directive (RoHS) by European Law in 2003, and they are controlled by a directive in the EU. In Finland, fish is the biggest source of PBB intake, however, levels of PBB in fish have been consistently well under the limit considered safe for human (Kiviranta 2012).

Polychlorinated napthalenes

PCNs consist of two benzene rings with chlorine atoms attached to the rings, forming altogether 75 congeners. They are used e.g. in electrical wires, wood preservatives, plastic additives, and lubricants for capacitor dielectrics. PCNs have been produced in the U.S. for over a hundred years, and knowledge of PCNs typically originates from occupational exposure (Hayward 1998). They are well known to exhibit health effects similar to dioxins and PCBs which include severe skin rashes and liver disease that in the most severe cases can lead to death (Flinn and Jarvik 1936; Brack et al. 2003; NICNAS 2002). Evidence for carcinogenicity is inconclusive (Ward et al. 1997). Fish is an important source of PCN intake in Finland, however, the daily intake on the population level is very low (Kiviranta 2012). The production of PCNs has been terminated since the 1980s but due to their persistence these compounds are still found in the environment, and therefore monitoring is advisable.

Organtotins

Organotin compounds (OTC) are ubiquitous contaminants in the environment, typically found in the aquatic ecosystems. They are compounds containing tin and hydrocarbon substituents forming dozens of complex compounds of which tributyltins (TBT) are considered to be the most toxic. Triorganotins are used as e.g. antifungal agents, agricultural fungicides, wood preservatives, miticides and acaricides (WHO 1990). Because of the antifungal properties, OTCs are also used in marine anti-fouling paint. This however allows OTCs to easily enter aquatic food web. Endocrine-disrupting effect is the most sensitive human health endpoint, and acute toxicity after dermal or oral exposure is considered to be low to moderate (Fromme et al. 2005). Hormonal disrupting effects have been seen in marine animals (EVIRA 2009). Fish is the major source of OTC in Finland, however the population level intake (0.007 µg/kg bw/d) is well below the TDI 0.25 µg/kg bw/d (sum of TBT, Dibutyltin, Triphenyltin, and Dioctyltin compounds), proposed by EFSA (EVIRA 2009). The first ban of antifoulant paints containing TBT came into force in 1986, and these control measures have successfully reduced the environmental concentrations (Waite et al. 1991). In 2003, Finland declared the total ban for the use of OTC as antifoulant agents in all ships (EVIRA 2009).

Lead

Lead has a very long history as an environmental pollutant. Exposure to lead can cause adverse health effects on nearly every organ and system in the human body, even death in extremely high exposures. Thanks to the successful regulations imposed on lead emissions (e.g. lead in petroleum was banned in many countries at the end of the 20th century), current environmental concentrations are much lower nowadays. The main health concern in the current lead exposure levels is damage to the nervous system of young children, and its potential to damage brain. Poisoning typically results from ingestion of food or water contaminated with lead. Inhalation is another possibly important pathway, particularly in occupational exposures. Hand to mouth behavior is a special exposure route for children. Lead is found in various food items, including fish, grain, vegetables, berries, milk, and meat products. In Finland, fish consumption covers approximately 22% of the total exposure to lead (EVIRA 2009).

Vitamin D

Fish is one of the few natural dietary sources of vitamin D. In Finland, lack of sunlight during the long and dark winter decreases skin's capability to produce sufficient amounts of the vitamin and therefore several food items (e.g. margarine, vegetable oils, low fat milk and milk formulas) are fortified with vitamin D.

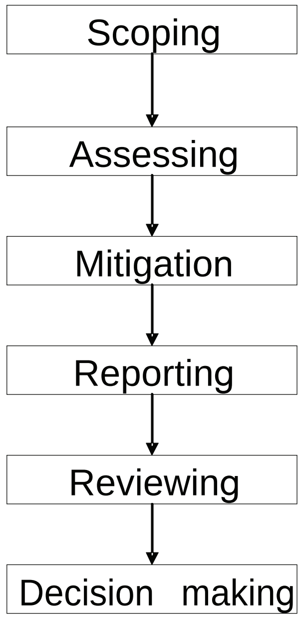
Vitamin D has been suggested to be beneficial to health in many ways, protecting against cardiovascular diseases (Wang et al. 2008), cancer (Autier and Gandini 2007), multiple sclerosis, rheumatism, metabolic disorder and type 2 diabetes (Mattila et al. 2007). However, evidence on cardiovascular benefits is still inconclusive (Pittas et al. 2010; Wang et al. 2010), the mechanism for multiple sclerosis is unknown (Ascherio et al. 2010), and also for cancer prevention evidence is inconclusive (Chung et al. 2009).Thus, despite many potential beneficial health endpoints of vitamin D, omega-3 fatty acid benefits are currently considered to be larger than those of vitamin D. Therefore, health effects of vitamin D intakes were not quantitatively evaluated in this work, but it would make an important addition to the future studies.

2.2 Assessment methods

This section closely relates to the practical question presented in the introduction of this work. *What explains the differences in conclusions of assessments?*

A common problem is that terminology related to assessments is confusing. Assessment methods in this work refer to different types of approaches, such as risk assessments, impact assessments, integrated assessments, and other endeavors used in assessing magnitude of health hazard, Mathematical modeling tools, such as Monte-Carlo simulation, Bayesian data analysis, and use of disability adjusted life years are regarded as assessments tools in this work.

In short, the differences in assessment methods rise from which aspects are considered in assessments. For example: concentration information only, risk estimate only, several risk estimates, or both risk and benefit estimates. An illustration of environmental impact assessment flowchart is presented in picture 8 (adapted from Ramsar project) as an example of a typical assessment process. A comprehensive collection of different environmental health assessment approaches and their contents is presented in Pohjola et al. (2012).



Picture 8. Flowchart of key steps in the environmental impact assessment procedure, adapted from Ramsar (2010).

Assessing risks stem from societal needs. There are many different assessment methods available in the field of environmental health assessment. Thus, one might ask what is the right way of assessing health outcomes in case of fish consumption? Is choosing the assessment method always case-specific or is one method generally preferred over the others? Ultimately, the purpose of conducting assessments should be providing research-based support to societal decision making.

The area of interest in this work is environmental health, area aiming at enhancing human health and well-being related to environmental issues. More specifically, fish consumption and human health. However, many of the methods presented here are used widely in different areas of life, e.g. in economy and technology. In the subsequent sections, fundamental terminology and methods on assessing risks and benefits will be introduced. Numerous different ways of assessing decision options where risks are involved have been developed. This literature review presents some of the common types of assessment methods; guidance value assessment, risk assessments, risk-risk assessments and benefit-risk assessments. General discussion of this work explores assessment methods more closely, especially their relation to fish consumption and health and decision making.

2.2.1 Scoping of assessments

Scoping, the starting point of an assessment is a critical phase where main questions and boundaries are defined. Scoping is vital for a successful process so that the work will focus on relevant issues instead of gathering scattered information. In other words, it serves in giving the assessment direction and structure. Typically, assessments with narrower scope tend to be more easily manageable and easier to interpret. Assessments with wider scope may be more laborious but can capture multifaceted views and better take into account societal needs. Basically all endeavors are subject to scoping.

2.2.2 Guidance value assessment

One could provocatively ask why we should eat anything that may pose risk to health. If fish consumption exposes a minor health risk, why face it if other sources of nutrition are available? It is important to realize that dose always determines poison. Consequently, we may ask: what is the limit value (e.g. concentration or intake) for defining something either safe or hazardous for health?

Finding safe levels of exposure to pollutants is a complex, time consuming toxicological challenge. It draws evidence from both animal experiments and epidemiological data. Because the focus of this thesis is on assessments and decision making instead of toxicology, closer analysis of how recommended intakes are arrived at non-cancer and cancer endpoints is only briefly introduced in this work (see section Risk assessments).

Table 3 presents a way how limit values are conducted from toxicological studies. Once limit values are available, guidance value assessment provides a simple method to compare concentration measurements with guidance values provided by different expert bodies. Guidance values can come e.g. in form of concentration or intake estimations. Intake calculations already hold an approximation of human exposure whereas concentration based measurements only consider the source. For this reason intake estimations can be theoretically considered as better determinants of risk and closer proxies than concentration measurements.

Biomarkers may provide useful, inexpensive and noninvasive choice for monitoring the exposure. Naturally, the choice of the biomarker (e.g. hair, nail, blood, placenta) used in the guidance value assessment should reflect the need of the assessment, and the biomarker should be measured accurately enough. Table 4 presented various guidance values presented in various units, provided by several different expert bodies.

Guidance values are generally derived by dividing the no-observed-adverse-effect level (NOAEL) or the Benchmark Dose Lower confidence limit (BMDL) by uncertainty factors, usually including a factor of 10 for inter-individual differences, and a factor of 10 for interspecies differences.

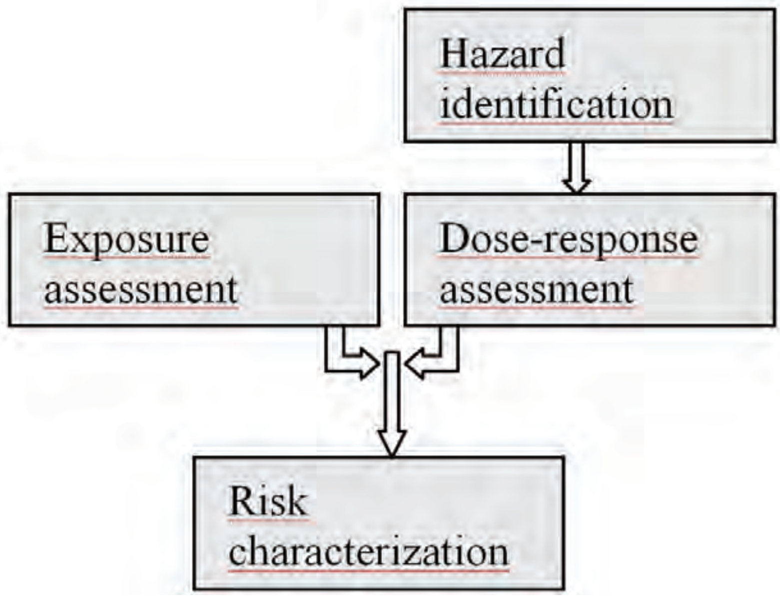
Guidance value is a useful tool for regulatory purposes. They can be used in identifying possible health hazards, which is the first step in the conventional risk assessment type presented next in this work. However, there is a difference in assessing whether risk exists or not, and conducting an assessment on how large the risk is. Moreover, guidance value approaches combine risk assessment and risk management by e.g including assumptions about shape of dose-response and/or applying precautionary principle.

2.2.3 Risk assessments

In 1983, National Research Council (NRC) established guidelines for performing risk assessments in the United States, commonly referred to as “the Red Book”. The purpose was to harmonize the way of conducting risk assessments in the U.S regulatory agencies. NRC has updated the risk assessment guidelines in 1993 (Pesticides in the Diets of Infants and Children), 1994 (Science and Judgment in Risk Assessment), 1996 (Understanding Risk: Informing Decisions in a Democratic Society), and 2009 (Science and Decisions). Also the U.S.EPA has been actively developing the risk assessment methodology and publishing guidelines (e.g. Risk Assessment and Management: Framework for Decision Making 1984, Risk Characterization Policy 1995, Risk Assessment Guidance for Superfund 1989).

According to the NRC (1983), risk assessment process consists of four steps: 1) hazard identification 2) exposure assessment, 3) dose-response assessment, and 4) risk characterization (picture 9). Noteworthy, risk management was strictly separated from this scientific process. This is to avoid scientific work getting influenced by political agendas. In the latest revision NRC (2009), this distinction is still considered important.

Risk communication is used for disseminating information to the public, groups and stakeholders. Together risk assessment, risk management and risk communication is referred to as risk analysis. Despite the fact that risk assessments have become increasingly complex and are nowadays being extended to address broader environmental questions, the description of a systematic process that separates risk assessment from policy-making and unifies the risk assessment guidelines can be considered as the cornerstone of contemporary risk assessment and it has been globally used in various endeavors.



Picture 9. Risk assessment proposed by the NRC (1983).

Hazard identification

In hazard identification, assessors investigate whether a stressor can cause an increase in the incidence of specific adverse health effect, and whether the adverse health effect is likely to occur in humans. With this information assessors evaluate whether to proceed to closer analysis of risk or just conclude that the risk is negligible. In hazard identification, weight of evidence based on the available scientific literature is also evaluated (U.S.EPA 2012).

Exposure assessment

Exposure assessment is a complex part and often a source of large uncertainties. Uncertainties stem from lack of knowledge, and it can be reduced by the use of better data. In addition to the limited understanding of effects and mechanisms in the human body, assessing the fate and transport of pollutants in the environment, knowing emissions rates or identifying sources are typical challenges in exposure assessments. For these reasons, exposure assessment is susceptible to biases and need to be carefully interpreted. Another challenge is to estimate frequency of exposure which adds on to the uncertainty of the exposure assessment. In case of fish consumption, the type of fish consumed, the frequency of consumption, and the meal size are some of the essential uncertainties contributing to the exposure (Domingo et al. 2007).

Variability is an inherent characteristic of a population. It can not be reduced but with improved information it can be better characterized. Because of the variation in the assessment variables, probabilistic methods become useful. They describe exposures as distributions, trying to take into account both high and low exposed individuals of the population.

Another source of uncertainty in exposure assessment is the longitudinal component. Often risk values are derived assuming a lifetime exposure but future exposures are not known. For example fish intake patterns change over a lifetime. Modeling is often limited to relatively short time period. Food consumption estimates (e.g. via food recall diaries, and food frequency questionnaires) suffer from difficulty in accuracy, and also with representativeness for a person's and population's long-term consumption. Probabilistic methods do help, but the data still faces the same limitations.

Exposure-response function

The exposure-response function comes in the form of a linear or nonlinear shape. Relationship defines the association of exposure and health endpoint. It is based on either epidemiological (studies on humans) or toxicological (studies on animals) data. Data may come from in vitro, in vivo, in silico, observational (e.g. case control studies and cohort studies) or experimental (e.g. clinical trials or intervention studies) studies (EFSA 2010a). Both toxicological and epidemiological approaches possess uncertainties but epidemiological data is preferred because interspecies extrapolation in toxicological data is considered a large source of uncertainty. NRC (2009) also emphasize that results of a dose-response assessment should be relevant to the problem being assessed.

Historically, U.S.EPA has been using different dose-response approaches for non-cancer and cancer end points. For cancer, no threshold of effect has been applied. This means that even the lowest doses increase the probability of cancer. For noncancer effects, a dose threshold (low-dose nonlinearity) assumption has been used. This in turn means that below a certain concentration (reference dose RfD, or reference concentration RfC) adverse effects are not expected to occur. The overall strategy was to harmonize cancer and noncancer approaches. However, this is a simplification not reflecting real life situations because noncancer effects do not necessarily have a threshold or low-dose linearity. Also the mode of action of carcinogens varies. Therefore the latest revision of the U.S.EPA risk assessment guideline (NRC 2009) suggests unification of cancer and noncancer dose-response assessment approaches.

Risk characterization

The main purpose of risk characterization is integrating information from the preceding steps, exposure assessment and exposure-response assessment and synthesizing an overall conclusion, often expressed as a risk estimate with attendant uncertainty. The U.S.EPA calls for consistency in risk characterization through transparency, clarity, consistency, and reasonableness (U.S.EPA 2000a). NRC (2009) encourages that risk assessments should better characterize and communicate uncertainty and variability. The result can be presented in various ways, such as incidences, lifetime excess risk, absolute risk, cost in money or with aggregate measures, such as disability adjusted life years (DALY).

Epidemiological studies

Epidemiology provides vital information for risk assessments, and therefore some basic concepts are briefly described.

Epidemiological study designs are prone to several biases and they are less controlled than animal experiments. In addition to common errors, systematic and random errors, epidemiological studies are associated with selection bias, information bias, and confounding (Sackett 1979). Selection bias relates to selecting study subjects. For example, cigarette smokers tend to differ in their participation rates (Sackett 1979). Mothers whose pregnancy ended in malformation, are more likely to report exposure to drugs than the control group (Sackett 1979). This is an example of information bias, more specifically recall bias. Confounding refers to co-occurrence of mixing of effects of extragenous factors (i.e., attributed to the wrong factor). The biggest difference between confounding and selection/information bias is that confounding stems from real causal effects.

Altpeter et al. (2005) aimed to propose minimum standards for practices and procedures that should ensure good quality and integrity of epidemiological research. They examined in detail 1) study protocol, 2) study conduct, and 3) publication of study results, and listed over 50 essentials of a good epidemiological study. In short, study protocol should be comprised of objective, hypothesis, population and sampling, data collection, statistical analysis, legal and ethical considerations, quality, resources and requirements, and early termination. Study conduct consists of prerequisites and responsibilities, information management, data handling, and documentation. The publication of study results is an essential part or the process because it disseminates scientific information to be dealt by other users.

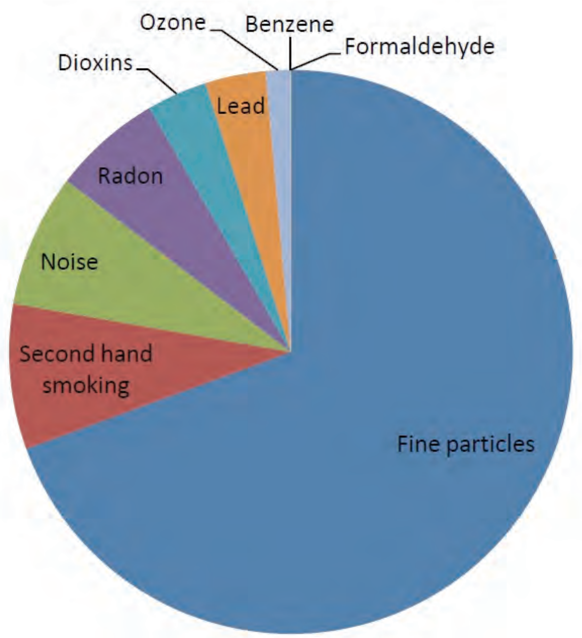
2.2.4 Risk-risk comparisons

Comparing risks provides better understanding of different risks in nature, and helps finding the optimal decision. Risk-risk assessments, often called as comparative risk assessments, are examples of these comparisons. Importantly, confrontations set the risks into new perspectives. The selected risks can basically be separately assessed using risk assessment method presented earlier.

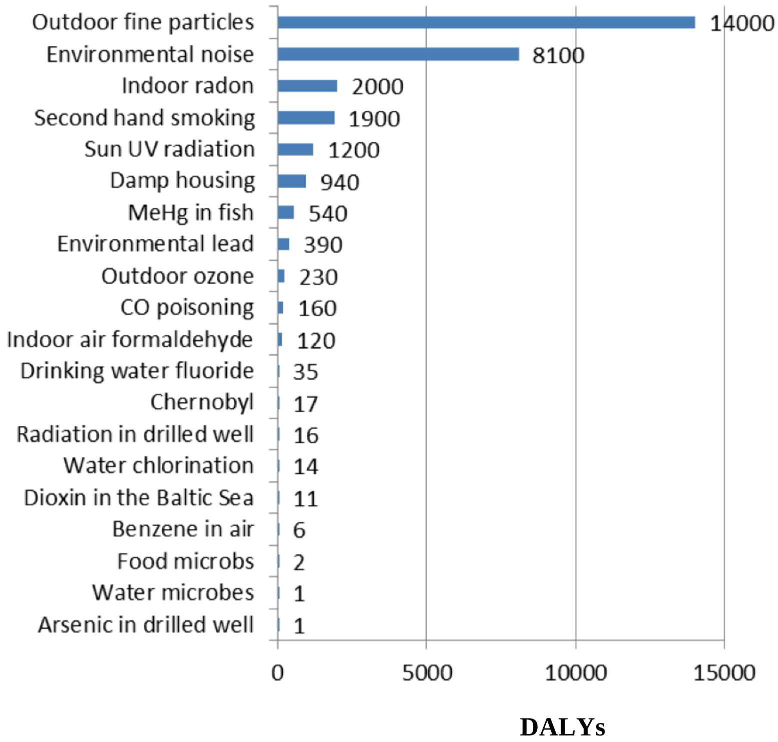
Comparative risk assessments can be simple comparisons of two stressors or larger multi-stressor assessments. In the latter one, ranking of the selected stressors is very useful information in the societal decision making. To avoid rise of public confusion and outrage, the risks compared should not be too remote from each other (Slovic 2000). For example, comparing mortality risks of living close to a nuclear power plant (radiation exposure) with driving car on a highway (accident probability).

In order to gain perspective about how large risk fish consumption poses to human health in Finland, two projects are introduced where contaminant exposure from fish consumption was included in the studies. First, EBoDE project, a collaboration of five European countries, analyzed a list of environmental stressors that are considered to pose the biggest threat to human health in Europe (Hänninen et al. 2011). The priority one category consisted of nine stressors: benzene, dioxins, environmental tobacco smoke, formaldehyde, lead, environmental noise, ozone, particulate matter (PM2.5), and radon. The results were translated into common metric, DALY, which will be explained later in this literature review. Picture 10 shows the results of the EBoDE project presented using non-discounted DALYs. PM2.5 was the leading stressor, associated with 6000 to 10000 DALYs per million people. Among the stressors considered by EBoDE, the health risk from dioxin exposure was medium or low. Further, EBoDE noted that the weight of evidence of dioxin carcinogenicity is weak. Annual mortality due to dioxin exposure in Finland was estimated at 30. The calculations were based on the same approach as applied earlier by Leino et al (2008), but they utilized a cancer slope factor that is approximately seven times higher than the one used by Leino et al. 2008. Further, the uncertainty in the estimate was considered to be large, and the upper confidence interval was estimated to be <500.

In Finland, a similar project called SETURI was carried out with the focus on nationally important environmental stressors (Hänninen et al. 2010; Asikainen et al. 2013). The project was a large national level collaboration between four Finnish research institutes (Public Health Institute, Institute for Occupational Health, Radiation and Nuclear Safety Authority, and Food Safety Authority). Picture 11 shows results from the SETURI project presented in DALY, and table 7 presented in number of cases. Dioxin exposure (mainly from fish consumption) pose only a minor risk to health (3.4 annual cancer cases, 95% confidence interval 0-35) compared to several other stressors, both expressed in lifetime excess risk and number of cases of adverse health effect. Burden of disease due to MeHg exposure from fish was considered moderate (figure11), but number of cases low (table 7). This demonstrates that burden of disease approach is able to capture different aspects of life than simple incidence information which may change priority of selected stressors (Asikainen et al. 2013).



Picture 10. Results from the EBoDE project presented in DALYs.



Picture 11. SETURI results presented in DALY (Asikainen et al. 2013)

Table 7. Results from the SETURI project presented in number of cases and endpoints (Hänninen et al. 2010).

Stressor	Number of cases/year	Adverse health endpoint
Fine particles	1600	deaths
Ozone	90	deaths
Passive smoking	480	coronary deaths
Damp housing	770	new asthma cases
Noise	90	coronary events
Lead	4	Mild mental retardation
Formaldehyde	26	nasopharynx cancer
Chlorination	14	bladder cancer
Carbon monoxide	10	death
Dioxin	4	All cancer
Methylmercury	28	mild mental retardation
Benzene	1	leukemia
Arsenic	0.1	bladder cancer
Fluoride	400	fluorosis

Lim et al. (2012) conducted a massive global burden of disease study including 67 risk factors. Similar to EBoDE project, they also utilized the DALY in reporting the results. Their conclusion was that the leading risks vary greatly across regions but worldwide a shift away from communicable diseases in children towards non-communicable diseases in adults is seen. The leading risk factors in Eastern Europe, most of Latin America, and southern sub-Saharan Africa were alcohol use, in most of Asia, North Africa and Middle East, and central Europe high blood pressure, in high-income North America and Western Europe tobacco smoking, and in Australasia and southern Latin America high body mass index. In sub-Saharan Africa childhood underweight, and in South Asia household air pollution were the leading risk factors. Lim et al. (2012) estimated that diet low in omega-3 fatty acid is attributable to annual 28199 DALY worldwide. Out of 67 risk factors in the study, low omega-3 fatty acid intake ranked 18th, right after total cholesterol (rank 15th), diet low in whole grains (rank 16th) and diet low in vegetables (rank 17th). High blood pressure was the leading risk factor worldwide. Moreover, Lim et al. (2012) showed that low omega-3 fatty acid intake seems to be a growing health concern.

2.2.5 Benefit-risk comparisons

Our environment is filled with substances that are both harmful and beneficial to health, an illustrative example being pharmaceuticals. They are designed for improving health but come with adverse side-effects. Chemicals and ingredients in food are no exception compared to pharmaceuticals. Rather, food is even more diverse issue because there are numerous ingredients in food items with both beneficial and adverse health effects. This gives a justification for conducting benefit-risk comparisons on food in order to find out optimal decisions.

Traditionally, the assessments of risks and benefits have been separate processes, and also the information communicated to consumers has been addressed separately. An extension to risk-risk comparison comes in form of benefit-risk assessment (BRA).

Food is controlled in several ways by both international (FAO, EFSA) and national (FDA, EVIRA) agencies. Their focus has traditionally been in increasing the understanding of potential health risks related to food, and providing guidance to consumers in terms of safe intake levels of harmful substances. They also provide intake recommendations of beneficial substances. In other words, they aim to guarantee the absence of food originated adverse health effects, and the sufficient intake of substances with beneficial health effect.

In managing BRA, decision makers will often have to tolerate some degree of risk in order to gain health benefits (Tijhuis et al. 2012a). In many studies, health benefits might have been acknowledged, however only qualitatively. For example, FAO/WHO (2011) concluded that the available data concerning special age groups, such as infants and children, is currently insufficient to derive quantitative BRA of fish consumption. However, quantitative benefit-risk comparisons would generally provide a more transparent way of estimating net health effects, and assist decision makers to make more informed and balanced decisions. Additionally, EFSA (2010) also promotes the concept of proper problem formulation in BRA in order to ensure useful and relevant outcomes of the BRA.

Research projects BEPRARIBEAN and BRAFO approached the question of how to make better BRAs. BRAFO suggested a tiered approach to be used in BRAs. BEPRARIBEAN produced six peer reviewed papers looking BRAs from different fields of science, including environmental health, consumer perception, food and nutrition, marketing and finance, food microbiology, and medicines (Pohjola et al. 2011, Ueland et al. 2011, Tijhuis et al. 2012a, Kelogeros et al. 2011, Magnússon et al. 2011, Luteijn et al. 2011, respectively). Additionally, the project produced introduction and conclusion papers (Verhagen et al. 2011 and Tijhuis 2012b). These can be considered as state of the art in BRA. The conclusions of these papers are summarized below:

- Assessment practices can still be characterized as relatively traditional risk assessment (Pohjola et al. 2012)
- BRA in medicine is a developed practice that is subject to continuous improvement and modernization (Lutejn et al. 2012)
- BRA tend to be skewed towards acceptance of all that is traditional and well-known, and rejection or suspicion towards anything that is novel (Ueland et al. 2012)
- BRA can systematically show current knowledge and its gaps, and provide answers to complicated questions with a large potential impact on public health (Tijhuis et al. 2012a)
- BRA could become a valuable methodology to support evaluations and decision making regarding microbiological food safety and public health (Magnússon et al. 2011)
- Predicting and explaining how market participants in the food industry form their overall attitude in light of benefit–risk trade-offs may be critical for policy-makers and managers (Kalogeras et al. 2012)

In 2010, EFSA presented a comprehensive guidance on BRA because guidance published (e.g. Aggett et al. 2005; WHO/FAO 2003; WCRF/AICR 2007) on how to perform benefit assessment of foods and food constituents was considered scarce. In this document they suggest dividing the assessment into positive health effect identification, positive health effect characterization (dose response assessment), exposure assessment and benefit characterization, which is analogous to risk assessment protocol suggested by the NRC (1983). Further, they suggest that BRAs should be comprised of three elements: risk assessment, benefit assessment and risk-benefit comparison. The document suggests to use BRA for example in a case where a single compound or food constituent has both positive and negative health effects.

Several sources promote using stepwise (or tiered) approach in BRA (EFSA 2006; EFSA 2010a; Hoekstra et al. 2008; Fransen et al. 2010). The advantage in stepwise approach is that at each subsequent step, the benefits and risks are balanced against each other to check if the assessment can stop because the risk/benefit balance is already clear. The higher the step, the more sophisticated methods are used.

2.2.6 Assessment principles

Assessments sometimes employ principles and tools that can be considered as components of assessments or guiding principles. Importantly, they carry features of built-in decision making, and valuations. Thus, policy choices may be inherently attached to these tools. Therefore assessor should be aware of impact of their use on decision making. Common metric and precautionary principle are presented as widely used examples of such tools.

2.2.6.1 Common metric

Common metric is a potential tool for presenting the results in a way that facilitates decision making. A simple application of common metric is expressing risks and benefits in the same unit, e.g. using mortality instead of morbidity e.g. cases of different diseases. However, this might not be able to capture all the burden of disease, and more comprehensive methods are usually needed.

Often, more than one metric will be needed to capture all dimensions of health. Only in cases with very large and clear differences between decision options, qualitative comparisons provide enough support for decision making. One of the typical challenges in benefit-risk and risk-risk assessments is that health endpoints are very different in nature (e.g. mood enhancement vs. cancer), often referred to as comparing apples and oranges. A more informative term for common metric approach in this case is common currency, which hints that some sort of exchange is performed to the units of outcomes. In this work common currency refers to metrics that have been modified applying established methods.

In cases where questions are value driven, there is a need for a transparent and easy-to-compare presentation of results. Common currency tool is able to reflect societal values which are incorporated into the outcome estimate. For example which disease is considered more serious over the other diseases, and how much more serious. In situations like these, applying severity weights become useful. Severity weights reflect the difference between utility in perfect health and utility in less-than-perfect health state. Severity weights can be derived in different ways (Dolan 1996), e.g. using time tradeoff questions, standard gambling, or health state dimension questions (mobility; self-care; usual activities; pain/discomfort; and anxiety/depression). Questionnaires can be addressed to community, patients with the conditions and experts/clinicians, and then analyzed. With the severity weights, burden of different health endpoints can be translated into a single metric, and they become easily comparable, providing useful information for the decision making.

Environmental economics and health economics are commonly used to estimate the changes in health states. There is empirical literature on willingness to pay (WTP) for reductions in mortality risk, which gives so-called value of a statistical life (VSL). This concept has been criticized for several reasons, for example because the estimates relate to the risk reductions of a sudden accidental death of working-age individuals (Kenkel 2003), and age dependencies and morbidity risks are less well-established (Dickie and Gerking 2002). Because of the obvious usefulness of the concept, there are several estimations for VSL available. For example, Tolley et al. (1994) provide monetary value estimation for each saved quality adjusted life years ($120000), and FDA (1999) estimated each life year saved by a nutrition labeling regulation at $100000. In the meta-analysis by Hirth et al. (2000), the median estimate of the WTP for a quality adjusted life year was about $265000. The U.S. EPA (1997) suggests a VSL estimate of $4.8 million. Based on cost-benefit-analysis (CBA) and cost-effectiveness-analysis (CEA), value of a quality adjusted life year range from $74000 to $450000 (Kenkel 2006).

Several European research projects (e.g. EFSA 2006, EFSA 2010a, BRAFO 2009, QALIBRA 2010, BEPRARIBEAN, PlantLIBRA, EBoDE) have tackled with common currency issues, and based on the experience from these projects potential candidates common currency measures have been acknowledged. In general discussion these candidates are presented in detail, where also the use of common metric/currency and valuations are further discussed.

2.2.6.2 Precautionary principle

Precautionary principle is not an assessment method per se, but not exactly a risk management tool, either. Rather, it is a policy approach for dealing with risks. Simply, if an action or a policy possibly poses risk to the public (or to the environment) and there is no scientific consensus about the existence or magnitude of the effect, the burden of proof falls in showing that the action is not harmful. In practice this means that actions to prevent/reduce hazards should be taken in case of uncertain information or lack of knowledge. There has been a debate over precaution which has riveted policymakers, scholars, business leaders, advocacy groups, and citizens. Some of the popularity in utilization of precautionary principle probably comes from pressure from the public.

Precautionary principle can be thought as a form of social responsibility from a decision makers' point of view. For example in the EU, precautionary principle has been made a statutory requirement. Wiener et al. (2010) studied the differences how precautionary principle is applied in the U.S. and Europe. They found that Europe has taken a more precautionary approach than the U.S. in risks such as genetically modified foods, chemicals, marine pollution, guns and climate change. The U.S. appears to be more precautionary than Europe regarding for example risks from lead in gasoline, drug approval, embryonic stem cell research, nuclear power, mad cow disease and terrorism. Although there is some evidence of a modest shift toward greater relative precaution of European regulation since about 1990, it very much comes down to societal valuations of countries to which risks precaution principle is applied.

Worst case scenario means that the most pessimistic perspective on future outcome is taken. Worst case scenario and precautionary principle may sound close concepts but precautionary principle poses a stronger argument. It is not feasible to apply precautionary principle to BRA because the precautionary principle would always (in cases where scientific understanding can be shown even slightly insufficient) suggest that risks outweigh benefits, whereas worst case scenario can be applied in benefit-risk calculations in a way that benefits are not overestimated and risks not underestimated. The outcome applying worst case scenario can still show that benefits outweigh risks.

Individuals often apply precautionary principle in decision making in form of "better safe than sorry" thinking, typically subconsciously. People are quite poor in comparing and judging different types of risks and precautionary principle is applied especially to those risks that are e.g. novel, man-made, catastrophic, and delayed by nature. This closely relates to risk perceptions which will be presented later in the next section. (Slovic 2010).

One of the challenges in laypersons' understanding of science is that there are different levels of evidence and consumers are not aware how to weigh this information. EFSA (2010) suggests that assessments should include a narrative of the strengths and weaknesses of the level of evidence and the associated uncertainties. This could perhaps better convey the message to the most educated consumers but generally consumers are quite poor in understanding uncertainties. Often uncertainty is perceived as a signal of risk (Paulos 1988). This in turn causes risk averse behavior. Still, information about uncertainties is vital to decision making. Also, (purposely) withholding this information from the public can really aggravate the situation if afterwards found out. As demonstrated, use of precautionary principle is a natural reaction to uncertainty.

2.3 Other interests

This section comes back to the practical question presented in the introduction: *What explains the differences in conclusions of assessments with the same topic?*

There are many other aspects of life that affect environmental decision making. It is virtually impossible to list all factors but this section tries to demonstrate that we have to be aware of their role in the decision making. Valuations in eating habits serve as an illustrative example of how different interests impact decision making related to fish consumption. For some consmers, hedonism alone determines their decision of what to eat. However, there are also several other factors involved in the decision making process of eating habits. As an eye-opener, a list of other interests associated with fish consumption (in alphabetical order) is described in table 8.

Table 8. Illustration of relation of other interests to fish consumption decision making.

Factor	Example
Cultural	Fish as a traditional dish
Ecological	Overfishing
Economical	Price of fish (meat)
Employment	Fair trade products
Ethical	Vegan diet
Hedonic	Taste of fish meat
Origin of fish	Domestic or imported
Political	Employment for fishermen

Table 8 gives various different valuations related to fish consumption. Cultural value of fish can be understood both as a special holiday delicacy, and as a part of regular daily meal. Price of fish meat and socio-economical are basically two sides of the same issue, valuation of eating fish. Ethical and ecological aspects are typically very individually driven aspects, whereas political and employment related questions need wider societal considerations. In questionnaire studies often hedonic values tend to be the most influential factor in the individual level decision making (Ueland 2012; Lappalainen 2012). A Finnish consumer survey (n=1300) studied the consumer behavior and valuations related to food (PTT 2012). The group found out that taste, domestic origin of food, price, and health were the most important factors for Finnish consumers. Additionally, the role of price of food has increased lately in the consumer decision making.

The interests listed in table 8 originate from personal, societal and political valuations. The obvious difficulty is how to quantitatively compare these valuations or evaluate their impacts on decision making. Assigning weights for table 8 factors would at least require applying some kind of common currency methodologies, and deriving weights for each factors. This would most probably be a very challenging and time consuming task.

Importantly, other interests can affect the whole assessment process, from the beginning to the end. Often these factors are considered as hidden interests, hard to recognize and quantify. Still, their impact may be huge, possibly driving the whole decision making. They are also found in the different societal contexts, from international to individual level decision making. On the individual level decision making, perceptions become particularly important and therefore this concept is presented in the next subsection.

The influence of other interests on decision making has been recognized by several researchers. Oken et al. (2012) studied different interests and valuations related to fish consumption advisories, including toxicological, nutritional, ecological, and economic points of views. Their finding was that despite the relative lack of information in integrating different interests, more comprehensive advice can and should be developed to describe the multiple impacts of fish consumption. Similarly, Pohjola (2013) also suggests that scientific research is only one input, sometimes a minor one, among all other inputs in the societal decision making.

The concept of other interests is close to the concept of systemic risks, defined in Renn and Graham (2005) as “the embeddedness of any risk to human health and the environment in a larger context of social, financial and economic consequences and increased interdependencies both across risks and between their various backgrounds.” OECD (2003) stated that risks systemic in nature need other assessments than simpler problems, including increasing linkages between science, policy and private sectors. The term “other interests”, however, more clearly reflects valuations and subjectivity involved in the assessments, and this term is therefore preferred in this work.

To simplify, multi-criteria decision making (MCDM) means that multiple criteria in decision-making environments are considered. It is a multi-disciplinary approach drawing knowledge from fields such as mathematics, behavioral decision theory, economics and computer technology. MCDM provide tools that help the decision maker to focus on their preferred solutions. The research on MCDM started in the 1970s (Köksalan et al. 2011). The concept of MCDM is also close to the concept of other interests used in this thesis, and can be considered as a structured attempt to quantify and compare the contribution of other interests in assessments. Various MCDM methods are described for example in Triantaphyllou (2000); Geoffrion (1972); and Steuer, (1986).

Also Knol (2010) studied uncertainties in complex assessments and suggested four types of risks. The fourth one, 'problems due to interpretative and normative ambiguity' is also closely related to the concept of other interests presented in this work.

2.3.1 Perceptions

Risk is perceived not solely by probabilistic numbers and technical parameters but also in our psychological, social and cultural context (Schmidt 2004). Our cognition works by combining new information with our pre-existing beliefs and values. Actually, we put more weight on the kind that supports our ideas rather than challenge what we already know (Hertz 2013). Because of the vast amount of information in the brain, cognitive thinking becomes very laborious and too slow to answer the needs in everyday decision making. Perceptions can be understood as instinctive ways of decision making, and they help people making fast and useful decisions based on their feeling, rather than cognition.

Perceptions manifest in form of peoples emotions, valuations and interests. Importantly, these feelings are also involved in the processes demanding cognitive thinking, such as in conducting assessments. These two different ways of thinking do not exist in separate universes but they both interact to our decision making process and behavior. Epstein (1994) was one of the first ones to label the two modes of thinking as "rational" and "experiential". Finucane et al. (2003) have poetically characterized this as 'the dance of affect and reason'. Despite the usefulness of perceptions in life and decision making, they come with several biases.

Psychological approach of risk perception research study the associations of psychological biases. A method called the psychometric paradigm, developed in the 1970's, quickly gained popularity (Slovic 2000). The psychometric paradigm is used to describe the way (lay) people judge risks. The basic idea is that perception of risk is quantifiable and predictable which makes it useful in analysis. It uses psychophysical scaling and factor analysis to produce quantitative representations or "cognitive maps" of risk perception (Slovic 2000). In psychometric paradigm, a group of parameters were identified, such as dread, controllability, voluntariness, familiarity, manmade vs. natural, delay effect and inequality (Schmidt 2004), which were found to affect the subjective estimation of risk (perception), causing strong biases compared to the actual measured risk. Moreover, there is correlation between these parameters, and often a large number of parameters can be compressed into one or two aggregate parameters in order to more clearly present the relationships. Sandman (1989) aggregated factors such as dread, voluntariness, controllability, lethality and fairness into something called 'outrage model'. Similarly, Slovic (2000) used factor analysis to aggregate 160 psychological parameters into twenty factors that reflect similar reactions. The key parameter (bias) in these theories is dread, and it has great influence on the individual level (and therefore further on the societal level) decision making. Importantly, studies using the psychometric paradigm have shown that it is possible to quantify and predict the perceived risk (Schmidt 2004).

Risk perception of food is a particularly interesting topic because consumers are very well aware about food entering the body, compared to other exposure pathways, such as inhalation and dermal, not to be sensed as easily. Ueland et al. (2012) found that consumers are particularly conservative in acceptance of foods. Traditional and well-known food is preferred and anything that is novel or highly processed is rejected, regardless of actual risk. ‘

In a recent questionnaire study, Ung-Lanki (2013) studied public perception of environmental health risks in Finland (random sample of 3000 Finnish-speaking persons, N=1112 responses), including perceptions of contaminants in fish. The questionnaire comprised of measures for perceived health risk, perceived exposure, self-reported sensitivity, concern and knowledge. One of the results was that perceived personal health risks of contaminants in fish ranked lower (mean value 2,45 on a scale from 1 to 5) than perceived general health risks of contaminants in fish (mean 2,97 on a scale from 1 to 5). Just as in this study, personal health risks are typically downplayed in comparison to general population health risk. This inconsistency stems from optimism bias (Weinstein 1987; Sjöberg 2003). Another example of the optimism bias is that smokers generally perceive personal health risk lower than the population health risk.

In addition to improving methods for eliciting opinion about risk, risk perception research affects societal decision making by providing a basis for understanding and anticipating public responses to health hazards, and improving the communication of risk information between laypeople, experts, and policy makers (Slovic et al. 1982).

3 Aims

This work has the following aims:

1. To estimate and compare major health risks and benefits originating from fish consumption
2. To estimate children's health risks from fish consumption
3. To find out factors contributing to fish consumption related human health assessments
4. To compare different assessment methods and their purposes
5. To discuss the challenges in societal decision making, particularly related to fish consumption

4 Methods used in the original publications

This part briefly presents how risk estimates were calculated and what materials were used in the original publications of this thesis. More specific information on methods can be found in the original publications.

4.1 Leino et al. 2008

Dioxins and airborne fine particles are both environmental health problems that have been subjects of active public debate in Finland. Moreover, legislation concerning exposure to both these contaminants is currently being updated. A comparative risk assessment of dioxins and PM2.5 was conducted, and in addition, a BRA of fish consumption. We chose the Helsinki metropolitan area as the geographical area of interest because this way full access to the actual road traffic data measurements performed in the Helsinki metropolitan area could be utilized. Moreover, fine particle concentrations in Helsinki are typically the highest found in Finland.

Emissions were used to estimate exposures under the different scenarios. Data for the emission submodel were received from a traffic emission model maintained by the Technical Research Centre of Finland (VTT). The emission model included annual fine particle emissions of all heavy-duty vehicles. Fine particle emissions were calculated using data on road and street traffic volume. Annual average population exposure to traffic-emitted primary PM2.5 in the Helsinki metropolitan area was estimated using two alternative exposure models. The first model was based on the EXPOLIS- Helsinki study, and the second was based on ULTRA study, in which the contribution of local traffic emissions was analyzed by using an absolute principal component analysis and multivariate linear regression.

The exposure-response coefficient for three mortality outcomes (cardiopulmonary, lung cancer, and other non-accidental) were estimated by using a combination of the result distributions reported in Dockery et al. (1993) and Pope et al. (2002). They assumed that the exposure-response function was linear without a threshold.

The fish consumption mediated dioxin risk estimate was calculated for the Finnish population and scaled down to the population of the Helsinki metropolitan area. The fishery catch data was obtained from the RKTL, and the pollutant concentrations of fish were obtained from the National Food Safety Authority of Finland. For dioxin cancer risk, we used cancer slope factor (CSF) as reported in the

IRIS database of the U.S.EPA, and assumed a linear exposure-response relationship for excess cancers associated with dioxin intake. For evaluating the concentrations of omega-3 fatty acids of sh species, we used the nutritional database Fineli, maintained by the National Public Health Institute, Finland (formerly known as Public Health Institute, Finland). We used database from Statistics Finland for demographics statistics and mortality data, accompanied with the WHO database.

For the calculations, Monte-Carlo method was used, a computerized mathematical technique that allows one to account for uncertainty in quantitative analysis and decision making. This method becomes particularly useful when modeling phenomena with significant uncertainty in inputs. The uncertain data inputs are random variables described by distributions. The model results are calculated by selecting X number of values randomly from these input distributions to produce an output distribution. In this work, Monte-Carlo model was implemented using the Analytica TM version 3.1.1 (Lumina Decision Systems, Inc., CA, USA) Monte Carlo simulation program. Latin hypercube sampling was used, and the model was run with 20,000 iterations.

4.2 Leino et al. 2013a

This work involved a BRA of fish consumption-mediated effects on central nervous system. The interest was the population level exposure. We created three separate fish consumption scenarios: mixed, lean, and fatty sh consumption. A fish body fat percentage level of 3% was chosen as a cutpoint of lean and fatty fish categories. The fat contents of fish and species-specific DHA concentrations in fish were acquired from the Fineli database, maintained by the National Institute for Health and Welfare. DHA intake was calculated as a product of the DHA concentration in fish (species speci c) and the consumption of fish (species speci c). IQ bene t estimate is a product of the DHA exposure and exposure–response function by Cohen et al. (2005c).

MeHg concentration data in fish was attained from EVIRA (Venäläinen et al. 2004). We used detailed consumption data for pregnant women (N = 3827) (EU-project BENERIS database). The data was collected for an EU-project BENERIS (Contract No. Food-CT-2006-022936) from two Finnish cities, Tampere and Oulu, and from their provinces. Because of both coastal and inland locations of the studied subjects, the data is considered to be a good representation of the Finnish population and the general Finnish fish consumption pattern. We first converted MeHg intake into the maternal MeHg blood concentration, and further into maternal hair MeHg concentration using single-compartment model, suggested and validated by the WHO and the U.S.EPA (Ginsberg and Toal, 2000), Two exposure–responses for MeHg were used, one proposed by Axelrad et al. (2007) and another by Cohen et al.

(2005b). Calculation of fish consumption mediated MeHg risk on the developing brain was done by using decline in IQ as an indicator. The risk was calculated as a product of pollutant concentration in sh (species speci c) and fish consumption (species speci c) which was further converted into MeHg concentration in maternal hair (using single-compartment-model) by multiplying with the MeHg exposure–response on IQ. The calculations summarized above are explained in detail in the original publication. The calculation was performed using Analytica TM version 3.1.1 (Lumina Decision Systems, Inc., CA), a Monte Carlo simulation program. Latin hypercube sampling was used and the model was run with 20,000 iterations.

4.3 Leino et al. 2013b

The objective of this work was to produce placental concentration data for an extensive number of environmental pollutants relevant to human health. This information can be further used in conducting risk assessments. Placentas were collected for studies called LUKAS-1 and LUKAS-2. LUKAS-1 was a Finnish EU-funded birth cohort study of approximately 200 children born in 2002-2004, and children in LUKAS-2 study were born during May 2004–May 2005. The aims of the LUKAS 2 study are to find out relation for early childhood living environment and childhood asthma. A total of 130 placentas were randomly selected from the study cohort for further analysis. Toxic equivalent quantities (TEQ), introduced in the literature review, for PCDD/Fs and PCBs were calculated.

17 congeners of PCDD/F, 37 congeners of PCB, 16 congeners of PBDE, 14 congeners of PCN, 19 congeners of PBB, p,p0 -DDE, seven OT compounds, ve heavy metals (Se, As, Cd, Hg, and Pb), and MeHg were measured. Before analyses, placentas were homogenized, and subsamples for POP, OTC, and heavy metal analyses were sampled. Subsamples for heavy metal analyses were delivered to the Technical University of Denmark. Placental subsamples for POPs and OTCs were freeze dried before extraction. The fat contents of placentas were determined separately from the same placental homogenates. The analysis protocols for POPs, OTs, heavy metals and MeHg are presented here briefly and described in detail in the publication.

In order to prevent bias in sample analysis, the placenta samples of POP compounds were freeze dried to remove water. Freeze dried placental samples were pulverized in a mortar and spiked with a set of 13C-labeled internal standards. After samples were extracted the quanti cation was performed by selective ion recording using VG-70 250 SE and Autospec Ultima (both from Waters) high resolution mass spectrometers (resolution 8000) equipped with Agilent HP 6890 gas chromatographs. The fat content of the placenta was determined gravimetrically from the obtained hexane. Concentrations were calculated with the lower bound method, where the results of congeners with concentrations below limit of quantification (LOQ) were designated as nil. OTCs were analyzed with gas chromatography–mass spectrometry, performed with an Agilent HP 6890 Gas Chromatograph connected to Waters Autospec Ultima high resolution mass spectrometer operated in the selected ion recording mode. All weights and concentrations of OTCs are expressed as OT cations. The diluted samples of heavy metals were analyzed using an ELAN 6100 DRC inductively coupled argon plasma mass spectrometer (ICP-MS) instrument. The concentration of MeHg from homogenized placenta samples was determined by ICP-MS

Intake distributions and statistical analysis were built using C-SIDE software (version 1.0; Department of Statistics, Center for Agricultural and Rural Development – CARD, Iowa State University, Ames), which implements the Nusser method.

4.4 Karjalainen et al. 2013

This work presents new information for assessing health risk of the most sensitive population subgroup of MeHg mediated health effects. Study subjects were participants in a population based cohort study called the Finnish Type 1 Diabetes Prediction and Prevention study (DIPP) where food consumption data of different children with varying ages was available. A background questionnaire and structured dietary questionnaires with 3-day food records were collected at ages 1, 3 and 6 years. Food records were available from 2858 children. All food records were collected during the years 2003–2005. The sh consumption of the children was recorded by their parents and day care personnel using 3-day food records. Food consumption was converted to ingredient level using in-house software and the Finnish Food Composition Databank. The majority of Hg concentration data for Finnish fish originated from a specific research project on Finnish fish, ‘‘EU-fish’’, in which 135 sh muscle samples without skins were analyzed for Hg using an established method. Statistical significance of the differences was evaluated using the Kruskall-Wallhis test.

MeHg intakes were calculated for 1-, 3- and 6-year-old children separately for both sexes using the calculated mean daily consumption of the sh containing food items multiplied by the corresponding mean values of MeHg concentrations. These intake distributions were estimated using statistical software C-SIDE. Total Hg analyzed from both domestic and imported sh was converted to MeHg using a conversion factor of 0.93. The assessed long-term mean daily intake of MeHg was compared with the PTWI of 1.6 μg/kg bw set by the FAO/WHO Expert Committee on Food and Contaminants and with the commonly used RfD of 0.1 μg/kg bw/day set by the U.S.EPA.

4.5 Pohjola et al. 2012

This work reviewed a concise set of environmental health assessment methods. This publication had a very different view because it compared assessment methods instead of quantifiable measures of health. The guiding principles in choosing assessment methods were that all the main areas and aspects of environmental health assessment should be covered. The assessment methods were evaluated based on the level of interaction; it was an adaptation of an approach developed by van Kerkhoff and Lebel (2006). Some of the included assessment methods have been explicitly developed to serve the needs of regulatory work, while some build more on the tradition of academic research.

The basic structure and the attributes of the framework were adapted from the PSSP (purpose, structure, state, performance) ontology (Pohjola 2003). The key attributes used in comparison of the assessment methods presented in the publication were purpose, problem owner, question, answer, process, use, performance and establishment. These attributes address the way each approach frames its purpose, issues of interest, assessment practice, linkage with use, as well as goodness of the assessment process and product. The framework for the analysis was created in order to guarantee a consistent scrutiny across the set of approaches, and to produce comparable characterizations. The results provide general description of contemporary practices and a basis for conclusions on the most essential aspects of environmental health assessment in terms of contemporary and future bene t–risk analysis, within environmental health as well as other domains.

5 Results

Table 9 aggregates the main results from the original publications 1-4. The main findings of the fifth publication are listed below table 9. More specific information on results is provided in the original publications.

Table 9. Key findings from the original publications I-IV

	Risk	Benefit	Conclusion
Leino et al. 2008	*1.2* annual cancer deaths from PCDD/F exposure (*10.5* pg WHO TEQ /kg bw/week), 34 premature deaths from fine particle exposure (*10.7* µgm^{-3})	*170* avoided annual CHD deaths (omega-3 intake), *25* avoided annual deaths (stricter emission standards for heavy duty vehicles)	Omega-3 benefit clearly outweighs dioxin risk. Fine particle risk substantially higher than dioxin risk.
Leino et al. 2013a	MeHg exposure (*3.6 x 10^{-5}* mg/kg bw/d) from lean fish consumption scenario poses a small risk on developing brain	Fatty fish consumption scenarios provides a small beneficial effect on developing brain	Fish consumption pattern of an individual determines the balance of benefits and risks.
Leino et al. 2013b	Concentration information of several environmental pollutants in placenta	Not assessed	Placenta concentrations dependent on parity and maternal age. Exposure sources of PCDD/Fs, PCBs, p,p0-DDE, and MeHg differ from the sources of PBDEs.
Karjalainen et al. 2013	1-15% of 1, 3 and 6-year-old children exceeded U.S.EPA MeHg RfD, respectively. Mean MeHg exposures from fish: *0.02, 0.027* and *0.044* µg/kg bw/day, respectively.	Not assessed	Finnish childrens' MeHg intake varied greatly between individuals and age. 6 year group intake was double the intake of 1 year group.

Key findings from the original publication Pohjola et al. (2012).

Future assessments have tendencies towards:

- increasing engagement between assessment and management as well as stakeholders
- pragmatic framing of assessments according to specific and practical policy needs
- integration of multiple benefits and risks from multiple domains
- explicit incorporation of both scientific facts and value statements in assessments.

5.1 Policy implications

Suggested policy implications arising from the original publications are presented in the following list.

- EU legislation serves in protecting the public health by giving strict emission standards for PM, and allowing consumption of herring and salmon from the Baltic Sea that exceed the limit concentration of dioxin in fish meat (Leino et al. 2008).
- Fish originated maternal MeHg exposures in Finland typically range between 0.03 and 0.06 µg/kg bw/d, well below the U.S.EPA reference dose 0.1 µg/kg bw/d (Leino et al. 2013a). However, the long-term mean daily intake of children (1-, 3- and 6-year-old) ranged between 0 and 0.331 µg/kg bw/d (above the U.S.EPA reference dose), supporting further monitoring of MeHg intake in children (Karjalainen et al. 2013).
- In Leino et al. (2013a) the benefit was found to offset the health risk of central nervous system of infants and children with mixed fish species diet. This means that fish consumption regulations promoting consumption of a variety of species is a safe recommendation. Fish consumption could be optimized in terms of health by consuming fatty fish with low MeHg. This, however, requires more consumer awareness.
- Placentas contain a cocktail of contaminants (Leino et al. 2013) but altogether they come in relatively low concentrations, and there is no obvious threat to the health of fetus, based on the concentrations measured and the current knowledge of the contaminants measured.

- Large variation in children's MeHg exposure suggests that there is a need to further consider children's consumption of fish high in MeHg (Karjalainen et al. 2013).
- Overall, fish consumption is beneficial to health if the official fish consumption recommendation (Finnish Food Safety Authority, EVIRA) is followed. Fish consumption mediated benefits and risks for sensitive population subgroups should be further studied.
- In order to facilitate decision making related to fish consumption, assessment methods need to be at the same time feasible but also include essential aspects of assessment and policy processes (Pohjola et al. 2011).
- Purpose and need should determine which assessment method to choose (Pohjola et al. 2011).

6 General discussion

Literature review presented the background and set the scope of this work, (picture 1). General discussion builds bridges between literature review and the original publications of this work, and discusses details. Fish consumption related health issues and societal decision involved form the substance in this work. In addition, the practical question stated in the introduction calls for identifying factors explaining the differences in assessment outcomes.

General discussion will also show how assessment methods, interests and perceptions together contribute to decision making. The original publications deal with interests and perceptions only superficially but their importance is particularly high when taking fish consumption issues out of the academic domain into the consumer level. Perceptions, presented in the last section in the general discussion, also pull together many of the features presented earlier in the thesis.

The content of the original publications were as follows: publications 1-4 (Leino et al. 2008; Leino et al. 2013a; Leino et al. 2013b; Karjalainen et al. 2013) demonstrated different ways of assessing safety of fish consumption and provide decision support. The first two publications focused on risk comparison, which is an effective tool in decision making. Actually, Leino et al. (2008) contained both risk-risk comparison, and benefit-risk comparisons. Leino et al. (2013b) and Karjalainen et al. (2013) dealt with the most sensitive population subgroup, children. The fifth publication, Pohjola et al. (2011) provided essential information about assessment methodologies, one of the three domains presented in picture 1.

6.1 Context of decision making

Decision making about fish consumption takes place in different societal contexts: internationally, nationally and individually. EU regulates maximum concentration of dioxins and PCBs in fish, and fine particle concentration in the air in terms of emissions from vehicles. However, Finland has been granted an exemption to sell fish exceeding the limit concentration for dioxins set by the EU. Decision support presented in Leino et al. (2008) is an example of international decision making process, with a national exemption. Conclusions presented in Leino et al. (2013a) can be used both in national and individual level decision making because it provides information for the consumption of fish species. Leino et al. (2013b) provides new information about fetal exposure, and Karjalainen et al. (2013)

presented children's MeHg intakes in Finland. These can be used in national decision making, especially for the vulnerable population subgroup, children. Pohjola et al. (2012) focus on analyzing the decision making and assessment processes, and this way contributes to international decision making.

How close the decision making of an individual is to national and international decision making varies between countries in form of public trust to authorities. Behavior of individuals is determined by both objective information and subjective valuations, and perceptions are key mediators in decision making of consumers. Perceptions also reflect societal valuations in both international and national decision making.

6.2 Fish consumption and health

Age is an important factor in fish consumption mediated health effects. Species-specific fish consumptions from table 1 with children's fish consumption reported in Karjalainen et al. (2013) shows that children seem to have similar fish consumption habits as adults. In both adults and children, consumption of salmon and gadiforms (saithe, cod, and haddock) is common. However, because of the smaller body weight of children, Karjalainen et al. (2013) found an increasing time trend in the estimated long-term daily MeHg intake with age up to 6 years. Maternal MeHg intake estimated in Leino et al. (2013a) was close to 6 year old children's intakes estimated in Karjalainen et al. (2013). Fish consumption patterns probably begin to differ at school age when children and their parents have different food for lunch.

In Finland, the concerns about fish consumption mostly relate to the Baltic Sea and POPs found in fish there. Because of the high fat content in Baltic herring and salmon together with lipophility of the pollutants, these species come with highest concerns. Interestingly, only 0.6% of salmon eaten by the Finnish population actually is caught from the Baltic Sea, the rest consists of imported and farmed freshwater salmon (Turunen 2012). Species consumed, and the origin of fish is of high importance in balancing risks and benefits of fish consumption.

Many of the heavy metals accumulate to aquatic life. Therefore their concentrations in fish are routinely screened. However, fish is not the only dietary sources of other heavy metals (other sources being e.g. nuts, cereals, meat and eggs). Depending on the form of heavy metal, fish consumption makes only up to 20 % (lead) of the total exposure on the population level, often much less (Hallikainen et al. 2010).

Fish consumption is the major source of placental exposure of several compounds, such as MeHg, dioxin and PCBs. Leino et al. (2013a) did not account for possible protecting effect of selenium against MeHg because the evidence is still inconclusive (Mercury 2006). However, the probabilistic model used in Leino et al.

(2013a) is constructed in a way that selenium effects could be easily incorporated later when toxicological information is available.

As presented in the literature review, several institutions have published recommendations on EPA and DHA intake. On EPA and DHA specifically, or for omega-3 fatty acid in general. In Finland, the average intake of omega-3 fatty acid is less than 200 mg/day (Aro 2009), below the WHO, EPA, and AHA recommendations. At the same time Finland is known to be a high fish consumption country. For these reasons, consuming supplements can be considered as a potential solution to increasing omega-3 fatty acid intake, especially for children and pregnant women who pose the greatest health risk from the contaminant exposure, and also the greatest benefits for the brain development. However, fish also contains other nutrients potentially beneficial for human health, such as vitamin D and selenium which are not acquired from a single supplement.

Consumption of fish as part of the diet should also be acknowledged. Fish meal is considered as an excellent dietary option, and if it is replaced by a dietary poorer choice, there might be negative health tradeoffs. Also Cohen et al. (2005a) and Oken et al. (2012) stressed out that unintended shifts in consumption can easily lead to public health losses. For example, households with pregnant women or young children in the U.S. reduced both their mercury and omega-3 fatty acid intakes after the 2001 fish consumption advisory. The omega-3 fatty acid decline occurred at not only among the targeted population but in all consumers. Moreover, even consumers with a college education did not differentially avoid high-mercury fish.

Typically, uncertainties in exposure-response functions are high. Leino et al. (2008) found that the largest sources of uncertainty in the model calculations were found in variables “does omega-3 help only CHD patients or everyone”, and “dose-response of health benefits”, not in the intake related variables. Similarly, in Leino et al. (2013a) exposure–response functions were responsible for the largest uncertainty in the model. Also value of information analysis in Leino et al. (2013a) revealed that the choice of exposure-response function is the crucial information in the model. This promotes further research on epidemiological evidence of fish consumption and human health.

Leino et al. (2008 and 2013a) and Karjalainen et al. (2013) showed the importance of what kind of fish is consumed. Pike, perch, pike-perch and burbot are the species with highest MeHg concentrations in Finland, whereas wild Baltic salmon and herring carry highest dioxin and PCB burdens. Therefore, benefits and risks seem to be highly dependent on which fish species are consumed. This is acknowledged also by Domingo et al. (2007) and Mozaffarian and Rimm (2006). Typically, lean fish consumption best corresponds to a person mostly consuming freshwater fish, and fatty fish consumption best corresponds to a person mostly consuming marine fish species. Further, marine fish species are typically both older and larger in size and therefore higher pollutant concentrations are accumulated to these species. Thus, there is great geographical variation in the Finnish fish intake patterns and these differences should be scrutinized.

6.2.1 MeHg and health

As pointed out earlier, there are great spatial differences in concentrations of pollutants in fish. It has been suggested that MeHg concentrations in Finland are higher in freshwater fish (Hallikainen et al. 2010), but findings in Karjalainen et al. (2013) were not able to confirm this. Still, MeHg concentrations in fish are probably higher in small freshwater ponds with both low water volume and acidic soil. However, their contribution to the average fish MeHg concentration in Finland is small because majority of the fish samples come from larger and less MeHg polluted freshwater areas.

WHO has published a practical guideline for assessing risks based on MeHg concentration in maternal hair (Poulin and Gibb 2008). It categorizes exposure into different exposure classes according to MeHg concentration in maternal hair. The adverse health outcome is defined as mild mental retardation (MMR) in offspring which incurs when IQ points decline under 70 points. First, the problem in utilizing this method is that maternal hair samples are often unavailable, as is the case in the original publications of this work. Second, and even more importantly, our intention was to measure health effects solely due to fish consumption and to exclude other sources of MeHg exposure (hair sample represents the total MeHg exposure). Third, the threshold of MMR set to 70 IQ points is more or less an arbitrary definition and it mainly serves regulatory purposes, not BRA that was the method used in Leino et al. (2013a). Incidence of MMR due to MeHg intake were used e.g. in SETURI project (table 7). As such, IQ provides an overall picture of child's cognitive health, and is a potential tool for RBAs.

Understanding the role of uncertainties is also important. For example, a big difference between MeHg and dioxin is that MeHg data come from epidemiological (and also toxicological) studies whereas the majority of information on dioxin comes from toxicology, especially for dioxin cancer endpoint. For many substances, including many of the pollutants considered in this thesis, toxicological information alone is considered not enough for drawing reliable conclusions on causality of human health effects but further evidence on effects in humans is required. These two study approaches are very different from each other. Typically, toxicological experiments on animals are well controlled where exposures can be accurately administered and measured. For obvious ethical reasons, we can not conduct similar experiments on humans but instead we have to rely on exposure information with large uncertainties. On the other hand, interspecies extrapolation is the major problem with toxicology which makes epidemiological information more desirable.

6.2.2 Dioxin and health

Dioxin research can be considered as an example of how complicated and laborious it is to study health risks of some chemicals. Despite the fact that dioxin research started already decades ago, there are many unsolved questions. This has also bogged down decision making based on risk assessment (The National Academy Press 2009).

Previously mentioned dioxin and PCB pollution episodes, such as Seveso (Bertazzi 1991), Yu-Cheng (Chen et al. 1992), and Yusho (Aoki 2001) have provided data for epidemiological studies of dioxins and PCBs. Dioxins were first considered human carcinogens. Also some more recent studies such as Bertazzi et al. (2001) support this. However, cancer as the most relevant endpoint for dioxin has been challenged e.g. by WHO (1998) and Dragan and Shrenk (2000). They proposed that TCDD is a promoting agent, rather than initiator. It promotes the growth and transformation of already initiated cancer cells but it does not cause mutations which may initiate a cancer cell. This would change the role of dioxin in risk assessments.

In 2001, U.S.EPA’s Science Advisory Board stated that there was no consensus on whether TCDD should be classified as a human carcinogen or whether the modes of action for animals and humans are similar (SAB 2001). Furthermore, they concluded that review of epidemiological, laboratory animal, and mechanistic data has led many scientists to support the threshold model for both cancer and non-cancer effects (SAB 2001, Pohl et al., 2002; Starr 2001). Current U.S.EPA cancer estimations are based on a linear, non-threshold model. Another provocative argument is that a certain level of AhR activation may be beneficial rather than harmful (Tuomisto 2006; Tuomisto 2012). This would mean that because of a J-shaped dose-response curve, low level exposure to dioxin would actually be harmless or even beneficial.

The U.S.EPA has been actively researching the toxicity of dioxins. The institute derived an estimate for cancer potency of most potent congener, TCDD, oral CSF of TCDD 150,000 $(mg/kg\text{-}day)^{-1}$ (U.S.EPA 1992). The more recent evaluation (Dioxin Reassessment) recommended using 1,000,000 $(mg/kg\text{-}day)^{-1}$ factor (U.S.EPA (2000b). Since the early 1990s, various CSFs spanning from 9,000 to 1,000,000 (mg/kg-day)-1, have been derived (Keenan et al. 1991, FDA 1993; U.S.EPA 2000b). Uncertainty in the cancer slope factor (CSF) offsets the three major factors, interspecies extrapolation, high to low exposure extrapolation, and data analysis techniques. Despite the many doubts in carcinogenicity, there is no current EPA guidance or policy that would constrain U.S.EPA to use CSF. The dioxin CSF 156000 $(mg/kg\text{-}day)^{-1}$ used in the study Leino et al. (2008) was purposely chosen as a conservative estimate in order to make sure that risks are not downplayed. In a way these dioxin results apply precautionary principle which can be considered reassuring in political decision making.

Developmental defects are currently considered to be the most sensitive dioxin human health end point. These effects should be included in the future dioxin risk assessments. Risk of developmental defects was the reason in 2013 for Norwegian Directorate of Health to temporarily reduce the recommended weekly farmed salmon consumption from two portions down to 1.5 portions. Later, this recommendation was critisized by other research institutes, e.g. National Institute of Nutrition and Seafood Research.

There are great challenges in studying developmental effects of pollutants. First, we lack understanding about the mechanisms and often also information about the chemical exposure. Second, it is very difficult or even impossible to show the causal association of early life exposure and disease later in life. Placenta is an excellent biomarker for fetal exposure and possible developmental defects. It was used in Leino et al. (2013b). However, the study only reported concentration information, not the relationship of pollutants and health effects. The levels of PCDD/F and PCBs, and number of placenta samples would probably be too low that an association between the pollutant concentration and developmental defects could be established. The best epidemiological evidence for developmental defects comes from studies conducted after Seveso accident, which showed deformation in the first molar teeth in PCDD/F exposed people (Alaluusua et al. 2004).

In dioxins and PCBs, the difference in concentrations between marine and freshwater fish is clear, concentrations being higher in the marine fish. Also, fat content of fish species range more than an order of magnitude between lean and fatty fish species (Hallikainen 2004; Hallikainen 2011). This is a big source of individual variation in dioxin exposure from fish, also acknowledged in Karjalainen et al. (2013).

Leino et al. (2013a) found that fatty fish consumption provides IQ benefits for children. However, fatty fish diet also might pose a health risk in form of developmental defects due to dioxin and PCB exposure. Thus, an elegant and simple fish consumption recommendation for children is not available but it is necessarily a tradeoff between omega-3 benefits and MeHg/dioxin risks. Eating a variety of fish species (Finnish fish consumption recommendation by EVIRA) tries to ensure that the exposures of harmful substances are averaged, rather than focused on one substance. At the population level, this seems to be a rational advice.

High correlations between congeners in both PDDD/F and PCB groups (Leino et al. 2013b) showed that instead of using full congener specific data, use of marker congeners gives a good estimation for the concentrations of other congeners as well as the TEQ. Therefore, marker congeners could be used as quick and inexpensive firsthand information in hazard identification.

In Leino et al. (2008), we used several conservative assumptions for dioxin risk estimation to make sure that the risk is not underestimated compared to the omega-3 benefit. In the end, benefits still clearly outweighed the risks, which make the health promoting conclusion stronger and decision making easier. However, it would be useful and interesting to redo the assessment applying best estimates instead of conservative ones. This could provide different information for the decision making.

6.3 Scoping

Scoping should be subject to the needs of decision making, not an attempt to make an assessment easier to manage. Importantly, scoping as the beginning of an assessment process may already determine the outcome of an assessment because many factors potentially changing the outcome of the assessment may already be excluded in this phase. Scoping should also ensure that its level of complexity is consistent with the needs of decision making. Also NRC (2009) confirmed that increased emphasis on planning and scoping leads to more useful risk assessments.

Exclusion criteria in scoping are typically given according to strategic plans of institutions, and it is conducted by a small number of experts, often the same persons conducting the assessment. However, there might be great benefit in gathering information from a wider audience because they might be able to bring in societally relevant questions the experts might not be aware of, e.g. by feeding in legitimate starting points, information about local economy or geographical/historical insights of the location. Depending on the assessment method, stakeholder involvement is taken into account with different emphasis. Participation especially relates to Pohjola et al. (2011) where various assessment methods were compared in terms of how participation is considered. It was found that in the emerging approaches there is a tendency towards increasing engagement between assessment and management as well as stakeholders, while the traditional and regulatory approaches mostly rely on closed assessment processes. Wiener et al. (2010) also acknowledge that much prior research has suffered from narrow or unrepresentative selection methods and other limitations.

NRC (2009) stressed out that greater up-front planning is required to ensure that relevant problems are being addressed. This in turn will give wider range of decision options. This again shows that an assessment does not properly serve the decision making if scoping phase is neglected, because interests of stakeholders, other interests and perceptions can greatly improve scoping for relevance. Because each assessment is subject to specific conditions, comparing scoping between different assessments is often not plausible. Importantly, scoping should be emphasized together with the conclusions of the assessment.

6.4 Assessment methods

This section discusses the roles of assessment methods. As a reminder, assessment methods are reflections of different societal needs presented in picture 1. Particularly interesting is how specific assessment methods affect the overall conclusions drawn from assessments, and ultimately the decision making.

Use of different assessment methods easily leads to situations where two different groups of experts with same research question draw different conclusions. For example, one research group conducting a BRA finds risk negligible and another group conducting an evaluation based on TDI finds exposure exceeding the limit value. Interestingly, both assessments may be solid pieces of work fulfilling the purposes set in the scoping phase. In this example, societal needs (by selecting the assessment method to be used) drive the conclusions for decision making (e.g. Tuomisto et al 2004).

Sometimes, unfortunately, information production per se becomes the center of attention in the assessments, rather than the practical needs of the decision making. This highlights the challenging role of environmental health assessment as mediators of scientific information into societal decision making, not only being self-contained scientific research. It is also emphasized in Pohjola (2013) that assessments should not be considered only as communication of results but identification of purpose and meaningful contextualization is required. This way effective collaboration between experts and decision makers is created. Further, Pohjola (2013) suggests that environmental health assessments provide a ground for developing methods and tools for science-based support to policy making.

6.4.1 Guidance value assessment

The ultimate goal in food safety is to protect public health, which sounds like a clear target. If there is a risk, it must be either avoided or diminished using regulatory measures. The literature review introduced several commonly used guidance values, such as TDI and allowable maximum concentrations. In order to fulfill the safety need, these evaluations often use worst case scenarios. The aim is to ensure that even sensitive individuals are on the safe side. Notably, guidance value assessments typically include several built in worst case scenarios, for example safety factors in dose-response functions and worst case scenarios in exposure assessments. The extreme end would be aiming at zero risk, which is almost in every case unrealistic, but still it tends to be a desired option. As an extreme example, there tends to be no public acceptance for radiation exposure from nuclear power plants, no matter how improbable the hazard (Slovic 2000).

A major challenge in giving fish consumption recommendations and guidance values for the public is that the health effects of beneficial and harmful substances are very much age-dependent. This makes clear and transparent communication challenging. For example, children and unborn children are more vulnerable to developmental defect risks due to MeHg and dioxin/PCB intake, whereas senior citizens would need to worry less about exposure to these pollutants but should try to ensure sufficient intake of omega-3 fatty acid in order to gain the cardiovascular health benefits. The official recommendation acknowledges children and pregnant women as a special population subgroup but closer speculation on age-specific fish consumption is not included in the recommendation. However, according to Finnish fish consumption recommendations by EVIRA, consumption of some fish species typically high in MeHg are suggested to be avoided during pregnancy. Exclusionary fish consumption recommendations like these were also suggested by Mozaffarian and Rimm (2006).

Results in Leino et al. (2013b) provide an example of information production for risk management purposes by presenting concentration information in human tissue. This tissue could be e.g. fish, hair, blood or any tissue with relevance in estimating health outcomes. Not much is known about fetal exposure to pollutants, but many xenobiotics can be transferred through placenta to fetal circulation. Therefore, placenta acts as a biomarker of fetal exposure, particularly important for pollutants with developmental toxicity, such as dioxins and PCBs. Guidance value method assumes that under a threshold concentration, typically set by an international body, the risk is negligible and above the threshold there are needs for actions in protecting the public. This brings us back to the question, "what is safe enough". Generally, lifetime risk of one case in a million is considered to be acceptable, even for the fatal outcomes. This is obviously a policy choice, not a scientific fact.

Another feature in determining the acceptable level of exposure is to add safety margins for no-adverse-effect-level (NOAEL). This approach originates from threshold concentration approach of adverse health effects, where below sufficiently low level exposure the expectation is to see no effects. In no threshold linear dose-response relationship approach even the smallest exposure increase the probability of adverse health effects. This is often the approach taken but there is no scientific evidence about what it has achieved in terms of risk reduction.

There is no way to decide on adequate safety margins scientifically – again, this is a policy choice. Therefore, in some cases limit values may be modified due to societal need and additional considerations. Guidance values set by the WHO and the U.S.EPA are examples of limit values but for example the EU legislation in outdoor fine particles varies because in the more polluted areas reducing concentration levels below the health based limit value becomes economically or politically not plausible (IIASA 2006). This is an example where other interests drive the decision making. An example related to fish consumption is described in Leino et al. (2008) where Finland was granted an exemption to sell fish exceeding the dioxin limit value because public health effects of BRA were considered to outweigh the risks. Also other interests and needs might have played a role in this decisionmaking.

Measuring concentrations in the environment and comparing the levels against the established guidelines and RFDs has the advantage of being simple and practical for regulatory purposes. As Oken et al. (2012) stated, clear and simple guidance are necessary to result in desired changes. Guidance value assessment answers this need. Karjalainen et al. (2013) used guidance value assessment in analyzing MeHg risk in children. For the majority, U.S.EPA reference dose was not exceeded but for a proportion of children (6-years-old girls and boys being the highest exposed age groups), long-term mean daily MeHg intake estimates exceeded the reference dose. This calls for further studies or actions.

Comparing guidance values to measured concentrations gives a general idea if there are health risks but it does not predict the number of health effects related to the exposure. Actually it is pretty close to the first part, hazard identification, in the traditional risk assessment approach, proposed by the NRC (1983).

6.4.2 Risk assessments

Risk assessments produce information to support decision making often using multidisciplinary approach. The results come with uncertainties, sometimes so large that the information becomes ambiguous. Another typical challenge is that the calculations are done by using uncertain quantitative, sometimes even qualitative, data. This statistical nature of the data is usually implemented by using probability distributions in the models. Academically speaking, often the most interesting finding of an assessment is not the conclusion or the single decision making but studying the uncertainty (Pohjola et al. 2012). This was also noted in NRC (2009) in terms of uncertainties leading to multiple interpretations and contributing to decision making gridlock. Uncertainty analysis promotes understanding of the key variables, provides essential information for decision making, and helps scoping similar assessments (Codex 2010).

NRC (2009) promotes the use of a novel approach, so called cumulative risk assessment. This term refers to broader public health and environmental health questions involving combined risks posed by e.g. aggregate exposure to multiple agents, aggregate exposure pathways and sources. The cumulative risk assessment idea agrees with the conclusions from this thesis. Again, the purpose of an assessment should define how the assessment is conducted. Cumulative risk assessment also stresses out the importance of formal stakeholder involvement process, which was also identified as a useful tool in decision making in this work. The concept is close to one applied in a Finnish environmental impact assessment approach, YVA. However, cumulative risk assessment still prefers to strictly separate risk assessment from political interference in the process by conceptual distinction between risk assessment and risk management.

Comparative risk assessments

Comparative risk assessments, where two or more risks are compared with each other, are informative for decision making. This was the approach used in Leino et al. (2008). Also, by ranking different risks, it is easier to make decisions on how to optimally manage societal health risks. This kind of information was produced in the SETURI and EBoDE projects. In the EBoDE project, dioxin risk was considered medium high but uncertainties were considered to be very large, and the risk estimate is possibly an overestimation due to conservative and pessimistic assumptions in the calculations (e.g. each cancer case was assumed to be fatal during the first year) (Hänninen et al. 2011). Also, the group utilized a very conservative estimation for cancer slope factor, seven times higher than the one used in SETURI. This explains the difference in the estimations from these two projects. Othervise, dioxin risk estimates in Leino et al. (2008) and SETURI are very close to each other.

One of the challenges in risk characterization is to choose an appropriate and transparent measure of outcome. Laypersons, even experts, have difficulties in understanding both probabilities and percent increases. Very small and very large numbers especially tend to lose their meaning the more extreme they get. Paulos called this phenomena "innumeracy", similar to illiteracy (Paulos 1988). Therefore, expressing risk in the form of number of adverse health effect cases brings better understanding. Fine particle risk estimated in publication Leino et al. (2008) is an example of outcome of a risk assessment where the increased probability of risk is transferred into number of adverse health effects in the given exposed population. This information should provide more transparent view to both decision makers and public.

Rise of public outrage from comparing risks too remote in nature often appears to be a thin red line. It would be useful to examine which psychometric parameters of risk tend to cause the outrage (perhaps at least dread and inequity). Comparing risks with similar psychometric dimensions could provide useful information for the societal decision without causing outrages. This is an example of the links from risk assessment to risk perception science.

6.4.3 Benefit-risk assessments

EFSA (2010a) concludes that benefit assessment should mirror the risk assessment paradigm by introducing four steps proposed by the NRC (1983). FAO and the WHO held an Expert Consultation on the Risks and Benefits of Fish Consumption in 2010. The tasks of the Expert Consultation were to review data on levels of nutrients (namely omega-3 fatty acid) and specific chemical contaminants (namely MeHg and dioxins) in a range of fish species, and to compare the health benefits of fish consumption and nutrient intake with the health risks associated with contaminants present in fish. It has been shown in number of studies that consumption of omega-3 fatty acid, acquired from fatty fish, lowers the risk of mortality from CHD among the general population (Mozaffarian and Rimm 2006; Kromhout 2012; Mozaffarian 2008; de Goede et al. 2010; Harris et al. 2008; Streppel 2008; Nordoy et al. 2001). Especially the elderly population is in higher risk for these diseases, and therefore they receive the greatest omega-3 intake health benefits. However, there are some studies not supporting the association of omega-3 fatty acid intake and reduced CHD (Kotwal et al. 2012; Smith 2012), and therefore omega-3 fatty acid health benefits as reduced CHD can still be considered challenged. There is also an absence of probable or convincing evidence of risk of CHD associated with low dose MeHg exposure (FAO/WHO 2011). As a conclusion, FAO/WHO expert panel promotes fish consumption, though maternal intake of dioxin-like-compounds should not exceed the provisional tolerable monthly intake, 70 pg/kg bw/month, set by JECFA.

Sometimes benefit-risk comparisons fail to give balanced information about fish consumption and health because there are differences in comparing risks and benefits:

1) Calculating risks is fundamentally different from calculating benefits. Toxicological dose-response function used for hazardous substances almost always entail safety factors but such factors are not used for beneficial effects. This in turn creates a bias that risks become emphasized compared to benefits. This is also acknowledged in EFSA (2010a) and Mozaffarian and Rimm (2006) where estimated CHD benefits are based on prospective studies and randomized trials in humans whereas estimated cancer risks include a 10-fold safety factor. An explanation for this bias is that the deduction of dose-response functions of hazardous substances have exclusively been serving the purpose of calculating risk-only type of assessments. An additional safety factor in risk estimate comes from interpolation from animal to human. One solution would be that benefit-risk comparisons should rely on the best available knowledge, not utilizing safety factors.

2) Health endpoints in BRAs are very different in nature, and therefore not easily comparable in decision making. Using common metric, such as DALYs, is a potential tool to this problem but especially laypersons sometimes feel uneasy with

it. If applicable, comparing similar health benefits and health risks is preferred. This was done in Leino et al. (2013a) publication where MeHg and DHA effects on central nervous system were compared using IQ as a common metric. In a situation where benefits clearly outweigh the risks, or vice versa, using common metric brings less additional value. This situation can be seen in Leino et al. (2008) publication where number of avoided CHD events is clearly higher than number of cancer cases (they were further translated into mortality assuming each cancer case to be fatal). Obviously, the diseases have to be somewhat equally serious so that the comparison won't be misleading.

3) In order to deliver balanced information for consumers and to see optimal public health behavior, benefits should be emphasized more than risks because information on risks is emotionally much more influential than that of benefits. This directly relates to perceptions and consumer behavior. Provocatively, we could ask what is the purpose of comparing benefits and risks if communicating them cause such a strong bias. Educating the public about this bias could be a solution to the problem, or taking this bias quantitatively into account in the decision making. After the information from BRA is delivered, it is pretty much up to individuals to choose which institutes, agencies, governments, experts, or lay persons they trust. In Finland, the trust for governmental research institutes is still is rather high compared to other countries but this trust can be damaged very easily (Bohnet and Zeckhauser 2003). For example, the controversial swine flu vaccination campaign managed by the THL led to decrease of institution’s trust in Finland.

As stated in the previous item, there is a common preference to err on the safe side when conducting risk assessments. The benefit-risk comparison of omega-3 fatty acid and dioxins in publications Leino et al. (2008) was based on using safety factors for risks because the prior assumption was that benefits outweigh risks. If benefits are still found greater than risks, conclusion can be safely made that the benefits outweigh the risks. Indeed, the benefits in Helsinki metropolitan area (one million inhabitants) were estimated to be 170 avoided annual deaths and risks 1.2 annual cancer deaths and it can be confidently said that the exemption for commercial fishing of herring and salmon serves the public health in Finland.

Hites et al. (2004) studied consumption of salmon using guidance value assessment as a method and concluded that there are health risks in eating farmed salmon that we need to be concerned of. As a response, Tuomisto et al. (2004) conducted a BRA on fish consumption mediated health effects and concluded that health benefits from omega-3 fatty acids in fish clearly outweigh dioxin risk of fish consumption and policy restricting salmon consumption would be detrimental to public health. This kind of dialogue is needed in order to improve societal decision making, and BRA is a useful tool for providing decision support.

Leino et al. (2008) and Leino et al. (2013a) conducted BRAs on dioxins and omega-3 fatty acids, and MeHg and omega-3 fatty acids, respectively. It was shown that the cardiovascular benefits clearly outweigh the dioxin risk. Also FAO/WHO

(2011) concluded that CHD benefits of consumption of fatty fish outweigh the potential cancer risks (U.S.EPA 2000b). In the case of MeHg and omega-3 effects on children's health, benefits compensated the risks. The main conclusion was that fish consumption pattern makes the difference whether fish consumption is slightly beneficial or slightly hazardous for the central nervous system of children. Also, Stern and Korn (2011) concluded that fish consumption advisories need simultaneously to address both omega-3 benefit and MeHg risk and that both are tightly linked through fish consumption.

Fish consumption BRA studies

There is plenty of fish consumption BRAs in the scientific literature. Some of the interesting ones with slightly different views are briefly presented below.

Sioen et al. (2007) study acts as an example of benefit-risk study utilizing reference doses. They studied the current intake of selected nutrients and contaminants via seafood in Belgian population. They concluded that the population did not reach adequate intake of omega-3 fatty acid, and MeHg exposure was not a major issue but TDI of dioxin-like compounds was exceeded among the heavy seafood consumers. Their approach emphasized the use of limit values.

To further investigate fish consumption recommendations and BRA, Scherer et al. (2008) conducted a comparative analysis of advisory web sites issued by U.S. states to assess health messages that sensitive populations might access. Their goal was to find out answers to questions 1) do fish consumption advisories also address the public health questions that sensitive populations face, 2) do advisories convey risk and benefit information on fish species, and 3) do they provide clarity for these complex risk issues? The group found complexity of assessing and communicating information about multiple contaminant exposure from fish consumption, communication regarding potential health benefits focused primarily on omega-3 fatty acids, and lack of both clarity and consistency in providing the information. Although the study was conducted in the U.S., it addressed an important point. The purpose of advisories is to serve the public health, and therefore benefits should be considered similarly with the risks. A similar conclusion was also suggested in Stern and Korn (2011). In addition, the group proposed a statistical approach in order to risks and benefits to be statistically disentangled and recombined to facilitate generalizable consumption advice. This could provide important information for assessing risks and benefits from different fish species.

Instead of simply comparing the health risks (MeHg) and benefits (omega-3) of fish consumption, Cohen et al. (2005a) studied the public health effects of changes in fish consumption habits. The study did not account for dioxins and PCBs, which especially in Finland would be relevant additions. They found that health benefits are gained if pregnant women were the only ones to reduce the consumption of high mercury fish species only. However, increasing the fish consumption of all members of the public (in the U.S) actually yielded the highest population health benefits. Importantly, if others than pregnant women also decrease fish consumption similarly (based on Oken et al, 2003 study) the population net health effect is negative. This shows the delicate balance in giving fish consumption recommendations. Therefore, consumer perception studies and carefully planned risk communication/management are of great importance.

When BRA is applied, its limitations and sources of bias should be acknowledged. Despite these challenges of BRA, using BRA has a great advantage of being able to estimate public health impacts of a whole ingredient or food item, rather than of a single substance. In case of fish consumption this is vital, as pointed out in Leino et al (2008) and Leino et al. (2013a). Because of this, BRAs should be given priority in societal decision making situations.

6.5 Common currency

Basically all ommon currency methods try to measure quality of life. Therefore they are efficient tools for decision making, providing aggregate measures of health effects. With these tools, decision makers can more easily compare options without a need for further valuations. Leino et al. (2013a) presented both risks and benefits using IQ, as an example of using common metric. Obviously, most of the time it is not possible to translate risks and benefits into a common metric this way.

Importantly, common currency itself is often a value statement because they include several assumptions and valuations, for example disability weights and age discounting. Below, a list of promising common currency candidates along with discussion of their use is presented, and further scrutinized in table 10.

- Incidences
- Disability Adjusted Life Years (DALY)
- Quality Adjusted Life Years (QALY)
- Days of work lost
- Costs in money
- Utility

Table 10. Summary table of common currencies options.

Parameter	Incidences	Disability Adjusted Life Years (DALY)	Quality Adjusted Life Years (QALY)	Days of work lost	Costs in money	Utility
Does it sum up to a single metric?	No	Yes	Yes	Yes	Yes	Yes
Can it be used for non-health endpoints?	No	No	No	No	Yes	Yes
What is the basis for weighting?	No weighting	Severity weight	Quality indices	Reduced capacity in the labor market.	Costs of treatment or willingness to pay to avoid a disease.	Decision maker determined on a scale from 0 to 1.
Where can the weights be used?	No weighting	Universally	Universally	Within a country.	Within a country	Only for cases with the same decision maker.
Who decides about the weights?	No weighting	E.g. an international panel of medical doctors	Large panels of patients and doctors.	Can be derived from medical statistics for a country.	Contingent valuation studies performed in a country.	The decision maker of each decision.
Are the weights easily available and usable?	No weighting	Yes, provided by WHO.	No, because based on capabilities and symptoms rather than diagnoses.	Yes for some countries	Rather easy for some countries.	Depends on decision maker's competence
Is the summary indicator easy to understand without further explanations?	Yes	Fairly easy	Fairly easy	Yes	Yes	No

To sum up the features and potential of all the common metric options presented in table 10:

- Incidences are calculated anyway in most of the health assessments, and they should be published anyway. Notably, because diseases and health conditions differ, incidence is rather a common metric than a common currency method.
- DALY is the preferred method, and better than QALY because of the easy availability of weights and diagnoses.
- QALY is also a good method and arguably more precise than DALY but because the purpose of many QALY based CEA studies is to help evaluate clinical intervention, many of the available QALY weights may not be relevant for the types of public policy questions. (compared with diagnoses in DALY)
- In many cases days of work lost is a practical metric, but ignores diseases in the young and elderly, and also varies between countries.
- If non-health endpoints are considered, money should be considered as DALYs are not applicable. It is widely used and thus makes comparison easy (at least within a country) but the value of money varies from person to person.
- Utility is the most comprehensive alternative, and any of the other methods can be seen as a sub-method for utility. However, because the application of utility is very much assessor driven, it is limited to a single assessment.

Many of the methods above have originally been developed for the economic evaluation of health interventions, not for environmental health decision making. Despite fundamental differences in the decision contexts and conceptual foundations of the approaches, different approaches often lead to similar policy decisions (Kenkel 2006).

6.5.1 DALY

The most promising candidate for the common currency measure is probably DALY, and therefore it is described in more detail in this section. Also EFSA notifies that choice of an aggregate measure, such as DALYs in expressing outcome of the BRA as a single net health impact value (step 3/3 in the EFSA 2010a approach), should first be justified. One of the advantages of using DALYs is that they represent a well established method for comparing health risks of different nature. Additionally, DALYs can also have a time-scale (EFSA 2006). In any case, care must be taken in the interpretation of the comparison, and the choice of aggregate measure should be made on a case by case basis, based on the specific risk-benefit question EFSA (2010). Burden of disease using the DALY approach can be calculated by two simple equations:

DALY = YLL + YLD
YLD = n x DW x L

, where DALY = disability adjusted life year (burden of disease), YLL = years of life lost, YLD = years lived with disease, n = number of new disease cases, DW = disability weight, L = duration of the disease

Obviously, there are challenges in using DALY. They can be applied only on the societal level, rather than on the individual level. Appropriate data for calculating DALY's may be unavailable. Importantly, clear messages are needed so that the numbers generated are not taken out of their context. Also, no generally applicable measurement scale is likely to be developed (EFSA 2006). It is also important to recognize that not all relevant dimensions are captured in the DALY approach. For example, although age weights can be applied, often simple unweighted values are used. This way DALYs do not reflect whether the effects are seen in adults or in children. Similarly, discounting DALYs provides a tool for adjusting effects in time but discounting is left out e.g. in sake of better transparency. Moreover, generally agreed metrics for positive health effects and well being are lacking and some of the weightings are under dispute (EFSA 2010a). EBoDE project studied a list of environmental stressors, and in addition to calculating incidence measures they translated the results also into DALYs. The results are presented earlier in the literature review.

6.6 Other interests

The original publications 1-5 of the thesis do not refer to the terms “other interests” or perceptions. The main reason for including these to this work is that they are relevatn inputs of *practical* societal decision making. They are inherently associated with assessments and research because value free decision making does not exist in real life. Despite other interests are inevitably present in the decision making, they are often disregarded by assessors. Without acknowledging other interests, the societal decision making process would be in most cases either incomplete or oversimplified. This part describes and discusses how underlying interests and perceptions interact with assessments and why they need to be taken into consideration in the decision making and risk communication.

Other interests can be important parts of scoping the assessment and choosing the assessment type. Broadly thinking, they can be simply thought as any input for assessments. As already pointed out, purpose should determine which assessment method can be used. Similarly, if the assessment scope needs to be wide, additional factors affect the choice of assessment method. For example, if an assessment was initially designed for assessing both human health risks and benefits, BRA would have been able to answer the need. But if stakeholders or other interest groups suggest that financial interests should have to be taken into account as well, standard BRA approach would not be able to capture all the essential features. Maybe a cost-benefit approach would provide sufficient tools to facilitate decision making in this example. It is important to understand what factors are involved in the assessment because it affects which assessment methods best fulfills the purpose of the assessment.

Lately, much work has been done in order to develop and harmonize how benefit/risk assessments are conducted (e.g. EU-projects INTARESE, BENERIS, BRAFO, BEPRARIBEAN). Also EFSA (2010a) emphasized that it is important to ensure that the outcomes of assessment are useful and relevant for the risk-benefit manager goals. Additionally, all this is influenced by other interests and valuations of assessors but how to incorporate these things into assessments? Open Assessment methodology and especially Opasnet tool appears to be a potential tool for this (Pohjola and Tuomisto 2011). It uses formal argumentation where both values and perceptions of experts and the public can be used in the assessment. The tool is not limited to academic purposes only but so far it has not been implemented in large scale public assessments.

Participation is one of the key mediators of other interests to assessments because participation feeds in interests from stakeholder involvement, it is also of a special interest in Pohjola et al. (2012). However, they speculate that sometimes participation is considered as an obligatory regulatory add-on without truly seeking for additional value from the process. Maybe for this reason, assessors tend to prefer to limit the scope so that the "inconvenient" interests are left out of the scope to be dealt with by someone else after the assessment has produced its output (so called someone else's problem). This demonstrates the two opposing mindsets:

1. Assessments are independent, narrow scoped, closed, expert driven scientific processes.
2. Assessments aim to capture variety of features involved in the societal decision making.

The reason for excluding factors from the assessment may be the difficulty in aggregating different endpoints (e.g. health, money, ecology, and ethics). However, there are means for comparing apples and oranges, as present in the section 'common currency' but the use of common currency often comes with challenges in transparency and communicating the results. This relates to the finding of Knol (2010) who stated that often assessments are too extensive and complex to perform but not extensive and complex enough to be useful. In the context of this work it means that due to the complexity in assessments, transparency may be lost but at the same time assessments are not able to capture all relevant interests. In other words, the reality is complex - we just have to find the best and the most useful ways in describing it. Similarly, mathematical models created in the assessments, such as presented in Leino et al. (2008) and Leino et al. (2013a), are only approximations on the reality and subject to framing and valuations.

Introducing additional factors to assessments often creates trade-off situations, and assessment outputs can not always be reasonably described using common currency. For this reason, assessors may try to avoid bringing these trade-offs to assessments, keeping the assessment as scientific and value free as possible, distinctive from subjective societal values. Another way of seeing this is that trade-off situations belong to the heart of societal decision making and including these add value to an assessment by reflecting societal valuations. This is also a reflection of democratic principles. Obviously, these two opposite ways of thinking (above presented 1 and 2) may produce very different conclusions.

A practical example about the importance of paying attention to additional factors in the assessments is fish consumption in Finland. As described earlier, fish from the Baltic Sea contain relatively high concentrations on dioxin and PCBs, particularly in salmon and herring. This is one of the reasons for the substantial decline of Baltic herring consumption in Finland during the last ten years (RKTL 2010). This has seriously impaired livelihood of professional fishermen, and the number of fishermen have decreased along with the decreased demand of herring. Fish industry is concerned about the situation, so their main interest is financial. On the other hand, environmental organizations are concerned about fish stocks of certain species found in the Baltic Sea, therefore their interest is ecological. Further, consumers are concerned about their health (both risk and benefits from fish consumption), so their interest is often health-related. There are also consumers living on the coast of the Baltic Sea who consider fish as part of their traditional food, so their interest is cultural. All these different interests produce valid arguments, but so far assessments have not been able to capture all these different interests. Instead of promoting their true interest, parties may have to use other interests which are easier to quantify or appeal stronger to people. All this results in unsatisfying decisions for all parties and may raise questions about hidden agendas (similar examples related to fish consumption presented in Oken et al. 2012).

Typically, institutions set strategies and objectives based on their fundamental valuations, policies and agendas. Also EFSA (2010a) states that BRAs require value judgments. These valuations can be publicly shared or given as preset scopes of the work. This ultimately determines what approaches and methods are used in the different institutions, which in turn affects the assessment outcome. Table 11 shows an example of value and scope comparison between different reseach institutes.

Table 11. Example comparions of other interests and values between institutes.

	Institute		
	Public health institute	**Food safety authority**	**University**
Aim	Public health	Safety of individuals	Information production
Ethical approach applied	Utilitarianism	Egalitarianism	Libertarianism
Methods applied	BRA / RA	Guidance value	Vary
Context of decision making	National	Individual	International
Conclusion	Estimation of health effects	Risk / no risk	Basically any new information

Utilitarianism as an ethical approach tries to maximize the benefits of the whole population. In case of fish consumption this means promoting public health by including both benefits and risks. Egalitarianism tries to protect all individuals equally, which reflects the use of guidance values in order to protect the all individuals. In libertarianism, the information needed is provided but the consumer decisionmaking is left for the individuals.

Other interests contribute to the decision making on several levels. Although the levels are more or less arbitrary, they exist at least on international, national and individual levels. On international level, there are interests such as political and legal (e.g. agreements on the international fishing areas), financial (e.g. foreign trade), and ecological (e.g. international quotas for endangered species). On the national level, cultural (e.g. fish as traditional dish), employment policy (e.g. subsidies for professional fishermen, and political (e.g. national regulations on fishing) are present. On international and national levels, interests are mostly bound to formal definitions, legal contracts, whereas in the individual level this can be explained by the consumer perceptions.

If the assessment method is chosen in a way that all interests can be incorporated into the assessment and societal needs are taken into account, better decisions and understanding could be achieved. Of course, doing this in real life is not a trivial task because assessments may become unmanageable. A potential tool and method for dealing with these types of assessments is previously mentioned Open assessment methodology and Opasnet tool (Pohjola and Tuomisto 2011). Also NRC (2009) promotes the idea of improving utility by ensuring that risk assessments are most relevant to the problems.

6.6.1 Perceptions

Risk perception often relates to things such as affect, intuition and heuristics. Although close concepts with other interests presented earlier, perceptions differ from other interests in one important way. Perceptions determine how person's emotions, valuations, intuition, and attitudes are reflected into behavior mostly through subconscious mechanisms, whereas interests can also be products of more objective and conscious reasoning.

Mozaffarian and Rimm (2006) concluded that confusion regarding risks and benefits could result in thousands of excess CHD deaths annually and suboptimal neurodevelopment in children. Although multiple nutritional benefits of including fish in the diet have become increasingly clear, concerns about pollutants have become more apparent in recent years. This again shows that understanding consumer perceptions is extremely important.

This section discusses how perceptions need to be considered in assessments, decision making and communication. The roots of risk perceptions stem from psychological biases, and therefore they act as a starting point for better understanding.

Roles of biases in risk perception

For many people the environment around us has never felt more intimidating than today. Despite the fact that most of us are unable to compare risks arising from natural or industrial origin, people feel threatened by emerging risks from new technologies and man-made substances (Slovic 2000), whereas all natural is generally considered safe. Similarly, Leino et al. (2008) suggested that the health risk from fine particles is perceived ubiquitous and therefore unavoidable, in a way natural. This is an example of applying heuristics in our everyday life. Statistically speaking, people in the industrialized world actually live longer and healthier than ever before in the history of man. Terms industrial and man-made are acknowledged as strong outrage factors and sources of bias in risk perception (Schmidt 2004). Industrially processed food in particular is perceived negatively (Leikas et al., 2009; Verbeke et al. 2007). Interestingly, despite the human inability to taste residuals of potent pollutants, such as dioxins in food, tasting attenuates perception of risk (Lähteenmäki et al., 2002). The preference of natural over man-made also reflects both the use of precautionary principle among individuals, and the dread of the unknown and uncontrollable.

Dread and lack of control are also acknowledged as key mediators of risk perception (Fischhoff et al. 1978, Verbeke et al. 2007). The public seem to be generally more concerned about dioxin in fish rather than fine particles in air, though the fine particle risk was found magnitudes higher in Leino et al. (2008) and both in EBoDE and SETURI projects (tables 6 and 7, picture 12) (Ung-Lanki 2013). The feeling of individual threat is often amplified by observing a number of possible minor hazards around us, no matter how unlikely and they are (Slovic 2000). This can also be seen in case of pollutant exposure from fish. Most consumers tend to assume additivity between the different pollutants so that both cancer risk from dioxin is emphasized because of the MeHg exposure and also IQ risk is emphasized because of the dioxin risk.

People’s perception is generally not related to concentrations of a chemical but simply to the presence of a chemical. Already almost five hundred years ago, Paracelsus discovered that only the dose determines if exposure is poisonous or not: "All things are poison, and nothing is without poison; only the dose permits something not to be poisonous" (Koulu and Tuomisto 2001). However, for most people already the presence of a poisonous substance is enough to create strong perceptions of risk.

Interestingly, the reasoning process for perceiving benefits and risks is different. Benefit perception is more based on heuristics and experience, while risk perception is based on cognitive information processing (Ueland et al. 2012; Fischer & Frewer 2009). This bias in balance of benefits and risks perception was noted also in FAO/WHO (2011). The bias reflects the need of prioritizing potential health risks by first identifying them, and after this health benefits are considered.

Consumers also tend to think that there is an inverse correlation between benefits and risks in food so that food perceived as highly beneficial is at the same time perceived as having low risk (Ueland et al. 2012; Slovic P. 1997). Zajonc (1980) and Slovic et al. (1997) similarly found the inverse relationship between benefit and risk perception, e.g. in the fields of toxicology and finance.

Media and risk communication

The importance of risk perception can also be seen in communicating risks/benefits and observing population's behavior. We can see that a good decision itself does not guarantee rational behavior of the population because the underlying psychological factors easily cause surprising public behavior.

Most of the people acquire information about health from the media and the Internet. Media is currently under a heavy competition which often forces to publish new and surprising findings that are designed to attract readers rather than provide balanced information. This easily gives the image of constantly changing information, which in turn raises confusion and threat among consumers. People are also surprisingly uncritical about what they find from the Internet, and they rather seek information that supports their beliefs rather than challenges them (Hertz 2013).

Fear is often the best method for selling products to consumers, and commercial media takes full advantage of this. Moreover, from the consumer point of view, media's role is large because there is a double bias on risks; media favors on publishing information about risks, and consumers tend to better absorb information about risks than benefits. Schmidt (2004) displays the challenging role of media and risk by an aphorism "Covered or not covered by the media? That is the question!"

A very common way of sharing information about hazard posed by chemicals is to list all the possible adverse health endpoints a substance poses on health, including the ones with less sufficient evidence or low probability of occurrence. By doing this public easily perceives causality from low dose exposure equally to all the listed adverse health endpoints. This is an effective way to purposely raise concern. One solution would be informing the strength of evidence on each health endpoint and reporting e.g. margin of exposures for all potential exposures. However, uncertainty is perceived closely associated to risk by the consumers (bias due to the unknown). For these reasons any person or institute sharing information on risks should understand that communicating risks is a very delicate matter that requires special attention and planning to.

Dioxins and MeHg serve as good examples demonstrating power of both dread and risk media. Dioxins were imposed with a strong stigma (Slovic 2000) during the Vietnam War, where they were used as contaminants in the U.S. military herbicidal warfare program. Second, after a chemical plant accident in Seveso 1976, information from animal studies began to blend in with reports from Vietnam. Phrases like "one of the deadliest chemicals known" and "the most powerful carcinogen known" were firmly established in the journalistic use of language (Severo 1979). Further, the dimensions of dioxin risks were summarized by Flynn et al. (2001) as 1) legal battles, 2) fear of pesticides, 3) accidents, 4) verbal over-dramatization, 5) failure to scientifically communicate risk, 6) emerging adverse health end points, and 7) power of civic organizations.

Perceptions and decision making

Risk assessments are to inform decisions, and therefore the intention should be in the direction of maximizing the utility of the population. On one hand, this is a question about efficiency in decision making (e.g. decision with small consequences), on the other hand about equity (e.g. decisions with possibly larger consequences). In terms of assessments, it is about understanding the purpose and acceptability of assessments.

As shown, most of the people take a very intuitive approach especially on food risks, by judging with perception rather than reasoning (Ueland et al. 2012). For example, consumers find it difficult to deal with the new information, and therefore tend to follow familiar ways instead of changing the eating habits (Ueland et al. 2012). Perceptions can be a challenge to researchers and decision makers if their power to people is not properly understood.

Importantly, perceptions are present throughout the assessment process and the societal decision making. For example, in choosing the assessment method, in scoping, in problem formulation, in choosing common currency severity weights, in individual level decision making, and in applying the precaution principle. Generally speaking, perceptions and subjective interests are always present when an individual or a group of individuals make decisions.

Both decision makers, assessors, and consumers are subject to risk perceptions and psychological biases. This raises several questions. 1) Should mechanisms of human behavior be taken into account already in the assessment process or should they be left to be dealt with after the decision making as risk communication? Incorporating the estimated effect of perception into assessments would mean adjusting the assessment outcome with the predicted behavior of the population. This way the well-being of the population could be better served. 2) Should the decision making follow the democratic principle by making decisions according to the opinion of the majority, even if it might be against their well-being?

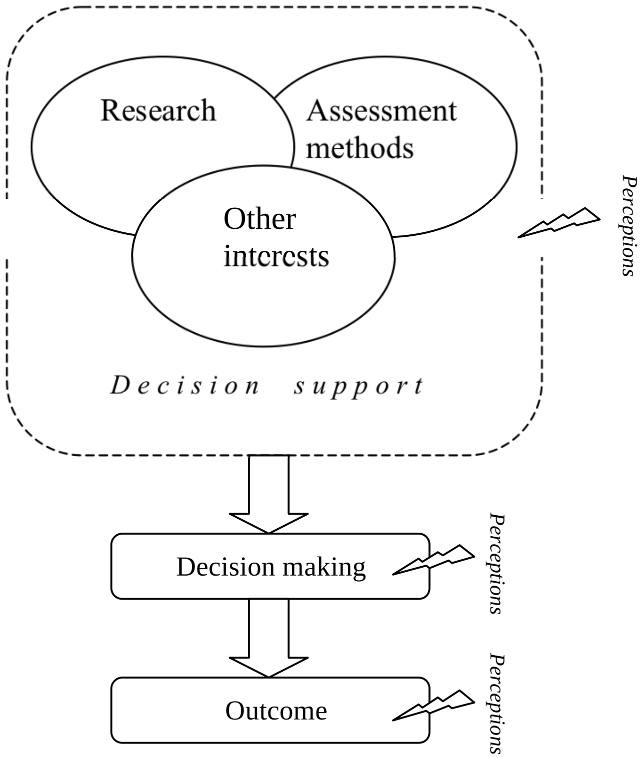
The importance of perceptions is hardly ever sufficiently considered in giving recommendations. However, this section strongly agrees with the FAO/WHO (2011) recommendation that fish consumption related risk management and communication strategies that both minimize risks and maximize benefits need to be further developed and evaluated. Understanding the role of perceptions is a critical part in this objective.

6.7 Summary

In addition in presenting current understanding of fish consumption and human health, this work tries to address a practical and a more general question: Why similar assessment questions may produce different conclusions. This further leads to fish consumption related societal decision making. Although, the main interest in this work is fish consumption and health, the question can also be extended to other areas as well.

All assessments (should) try to address a specific need, which usually is to improve the well-being of the society. In this work, I have divided the work using three main domains; research, assessment methods and other interests.

Outcomes of assessments are not only results of objective scientific data and reasoning but importantly, there are many things involved in the assessment process. Picture 12 summarizes the thesis in the form of a mental map. At the top of picture 12 stands picture 1 but it comes with a small modification. In order to link the general idea presented in the picture closer to the context of this work, societal needs are called 'assessment methods'. Together research, assessment methods, and other interests form the decision support which feeds decision making. After decision making outcomes will be seen in the society, which should be the ultimate goal in conducting assessments. Contributions of perceptions come in different phases. Assessors' perceptions affect decision support, decision makers' perceptions affect decision making, and consumers' perceptions affect outcomes seen in the society.



Picture 12. Illustration of factors in decision making

7 Conclusions

This section integrates literature review, original publications and general discussion parts of this thesis by listing the main findings of fish consumption and health, assessments methods, and related decision making. Other interests and perceptions are adherent to all these domains.

Fish consumption and health

- Fish consumption in Finland does not pose major health risks to the consumers. Rather, there are health gains in fish consumption.
- Fish contains several pollutants. In Finland, only few of them (MeHg, PCDD/F, PCB) are found in concentrations that require closer analysis, e.g. risk assessments or BRAs.
- Fish consumption is the predominant source of MeHg exposure, and MeHg exposure can attenuate DHA health benefits.
- Benefits and risks are highly dependent on which fish species are consumed. Moreover, distribution of health benefits and risks are very age-dependent.
- Studying the most sensitive population subgroup is important but general fish consumption recommendation makes the biggest contribution to the public health.
- A small proportion of young children in Finland are exposed to MeHg levels exceeding the U.S.EPA reference dose. Further monitoring program especially for susceptible subpopulations, children and pregnant mothers, is advisable.
- Communicating health risks and benefits are very delicate matters. Special attention should be paid to balanced information production of both risks and benefits, and acknowledging biases.

Assessments and decision making

- Scoping and choosing the assessment method strongly affects the outcomes of assessments and the decision making. Therefore, their selection should be based on explicit expression of purpose and needs of the decision making.
- Other interests are involved in the whole chain of assessment, and incorporating them into assessments may provide additional value to the societal decision making. The purpose of the assessment also determines the need for accounting for appropriate interests.

- There is a tendency towards BRAs instead on risk-only assessments in fish consumption health studies. Assessing benefits may come with challenges but benefit assessment is often an essential part in the decision making.
- Despite the challenges in transparency, aggregate health measures are useful tools in the decision making.
- The role of scoping should be emphasized together with the conclusions of assessments.
- Special attention should be paid to the role of consumer perceptions. It is a key for successful societal decision making.

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