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Benefit-risk assessment of fish and fish products in the Norwegian diet - an update

Opinion of the Scientific Steering Committee of the Norwegian Scientific Committee for Food Safety

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An update of the benefit-risk assessment: A comprehensive assessment of fish and fish products in the Norwegian diet – based on new knowledge

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Assessed and approved

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Competence of VKM experts

Persons working for VKM, either as appointed members of the Committee or as external experts, do this by virtue of their scientific expertise, not as representatives for their employers or third party interests. The Civil Services Act instructions on legal competence apply for all work prepared by VKM.

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Summary

Request from the Norwegian Food Safety Authority (NFSA)

In September 2013, the Norwegian Food Safety Authority requested VKM to update relevant parts of the benefit-risk assessment of fish in the Norwegian diet published by VKM in 2006. The background for the request was new knowledge and data on the content of some nutrients and contaminants both for wild and farmed fish since 2006. The proportion of vegetable ingredients used in farmed fish feed has in recent years increased, and new national dietary surveys for adults and children have been conducted.

The Norwegian Food Safety Authority referred to VKM's report from 2006, which pointed out that the positive impact of fish consumption on public health was especially due to the content of polyunsaturated fatty acids and vitamin D in fish. Further, VKM concluded that the contaminants that could pose a potential risk to public health through fish consumption mainly were methylmercury, dioxins and dioxin-like PCBs (dl-PCBs).

The request included a reassessment of fish consumption in Norway with focus on specific nutrients; n-3 fatty acids (eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), docosahexaenoic acid (DHA)), vitamin D, and the minerals iodine and selenium, and on specific contaminants; mercury, dioxins and dl-PCBs. VKM was asked to address the main changes in the use of raw materials in farmed fish feed and how these affect the levels of nutrients, mercury, dioxins and dl-PCBs and in fish feed. Further, VKM was asked to address to what extent levels of nutrients and contaminants in fish have changed since 2006, to describe these changes and estimate the human intake of the substances in question on the basis of recent dietary data. VKM was also requested to consider the benefits of eating fish with regard to the intake of nutrients and the risks associated with the intake of mercury, dioxins and dl-PCBs and comment on whether this change the conclusions from the report in 2006. Additionally, on the basis of updated knowledge, VKM was asked to comment whether other substances, like pesticide and residues of veterinary medicinal products, could affect the conclusions with regard to the impact on public health.

The Norwegian Food Safety Authority and the Directorate of Health will use the updated assessment as a basis for public recommendations concerning the consumption of fish and fish products.

How VKM has addressed the request

The VKM appointed a working group consisting of VKM members and external experts to answer the request. Several of the scientific panels of VKM reviewed the report during its preparation. The Scientific Steering Committee of VKM has given their final assessment and approval of the current report.

In the current report, VKM has mainly used data from national surveillance and monitoring programs for nutrient and contaminant concentrations in fish feed, farmed fish and wild caught fish, but occurrence data have also been derived from peer reviewed articles.

VKM has estimated fish consumption in three population groups (2-year-olds, adults and pregnant women). The estimated fish consumption was compared to national dietary guidelines.

To assess health effects of fish consumption, the current estimated fish intakes were also compared with assessments done by recognised international bodies and results from epidemiological studies addressing possible associations between fish consumption and specific health outcomes. Literature searches were done to identify relevant epidemiological studies. VKM has not systematically assessed reviews or meta-analyses nor individual studies for weight of evidence, but merely summarised the studies retrieved from the literature search. It was considered being beyond the scope of this assessment to review individual studies included in reviews or meta-analyses.

Furthermore, based on current fish consumption in the various population groups, intake of nutrients and exposure to contaminants from fish were estimated. For benefit characterisation of the specific nutrients the estimated nutrient intake was compared with national recommendations of nutrients intake and for EPA and DHA a comparison was also done with European recommendations. For risk characterization of contaminant exposure from fish, VKM used health based guidance values set by international risk assessment bodies (WHO, EFSA).

VKM noted that the request from NFSA was restricted to fish, whereas the VKM report in 2006 included both fish and other seafood.

VKM focused on specific nutrients and contaminants as requested by the NFSA. In addition, VKM also commented on other substances that could affect the risk assessment, such as residues of veterinary medicinal products including residues of antibiotics, new contaminants from fish feed like the pesticide endosulfan, polycyclic aromatic hydrocarbons (PAHs), mycotoxins, the synthetic antioxidants ethoxyquin, butylhydroksyanisol (BHA) and butylhydroksytoluen (BHT), as well as environmental contaminants like brominated flame retardants and perfluorated organic compounds.

Background

In the Norwegian diet fish is important source of well-balanced proteins, and important nutrients such as EPA and DHA, vitamin D, iodine and selenium. On the other hand, fish is also a source of exposure to chemical contaminants like dioxins, PCBs and mercury.

Over the last 10 years there has been a great change in raw materials used in fish feeds, and in 2013 terrestrial plant proteins and vegetable oils accounted for 70% of the feed. The changes in concentrations of nutrients and contaminants in fish feed for farmed Atlantic salmon and trout are reflected in changed concentrations and compositions of the same nutrients and contaminants in the farmed fish fillet.

The current national dietary guideline is to eat fish as dinner meals 2-3 times per week for all age groups, representing 300-450 g fish per week for adults, including at least 200 g fatty fish, such as salmon, trout, mackerel and herring. Fish is also recommended as bread spread. Further, a daily supplement of vitamin D to infants from 4 weeks of age is recommended, and if this supplement is taken as cod liver oil it will in addition ensure an adequate supply of EPA and DHA.

The present benefit-risk assessment is comprised of three elements, i.e. benefit assessment, risk assessment and benefit-risk comparison. This methodology is in accordance with the guidance given by EFSA in 2010.

Fish consumption in Norway and comparison with national dietary guidelines

VKM has used information about fish consumption from more recent national dietary surveys among 2-year-olds (Småbarnskost 2007) and adults at 18-70 years of age (Norkost 3, 2010/2011), as well as information for pregnant women who answered the Norwegian Mother and Child Cohort Study (MoBa2, 2002-2008) food frequency questionnaire. The national food consumption survey Ungkost 2000, which covers the age groups 4-, 9-, and 13-year-old children, was considered too old to be used and it is therefore not known if their fish consumption patterns have changed, neither in amount consumed nor type of fish consumed.

Even though there are methodological differences between the dietary surveys used in 2006 and 2014, the amount of fish consumed appears to be unchanged for all population groups. Furthermore, in 2014, lean fish and fatty fish contribute with about 60 and 40 percent, respectively, of the total fish consumption, which is similar to 2006.

Given a portion size of 150 g fish, the average adult eats fish equivalent to 2-3 dinner servings per week and the average pregnant woman eats fish equivalent to 1-2 dinner servings per week, while the average two-year-old eats fish equivalent to 1-2 dinner servings per week given a portion size of 75 g. The table below describes fish intake in the selected populations.

Fish consumption (expressed as raw fish), mean grams (g) per week in 2-year-olds (Småbarnskost 2007, n=1674), adults (Norkost 3, n=1787) and pregnant women (MoBa, n=86277)

Population groups	Mean fish consumption g/week			Fish roe and liver
	Fish, total	Lean fish (\leq 5% fat)	Fatty fish ($>$ 5% fat)	
2-year-olds	112	70	35	7
Adults	364	210	147	7
Pregnant women	217	126	77	14

VKM concludes that of the different population groups, only adults (18-70 years of age) with an average or higher fish consumption reach the national food based dietary guidelines for total fish consumption. Mean total fish consumption and fatty fish consumption in children (2-year-olds) and pregnant women, as well as the mean fatty fish consumption in adults are lower than recommended. In pregnant women and 2-year-olds, fish consumption is too low to meet the food based dietary guidelines.

Health effects of fish consumption

VKM is of the opinion that according to epidemiological studies, the net effects of the present average fish consumption in Norway for adults including pregnant women is beneficial for specific cardiovascular diseases (particularly cardiac mortality, but also with regard to ischaemic stroke, non-fatal coronary heart disease events, congestive heart failure and atrial fibrillation), as well as for optimal neurodevelopment of foetus and infants. Furthermore, VKM is of the opinion that those with fish consumption less than one dinner serving per week may miss these beneficial effects.

The health benefit of fish consumption is reported from 1-2 dinner servings per week and up to 3-4 dinner servings per week. For higher fish intake per week, the limited number of consumers in epidemiological studies does not allow for drawing firm conclusions about the actual balance of risk and benefit. More knowledge is needed to reveal the beneficial mechanisms of fish consumption.

Benefit characterisation of nutrients in fish

VKM is of the opinion that there has been minor or no changes of the composition and concentrations of nutrients in wild caught fish since 2006.

Due to replacement of fish oil and fish protein with plant proteins and vegetable oils in feed for farmed fish, the concentrations in farmed Atlantic salmon with regard to EPA, DPA and DHA, and selenium are about 50 and 40% respectively, of the corresponding levels in 2006, while the concentration of vitamin D appears unchanged. The level of iodine in farmed Atlantic salmon was low in 2006, and is still low compared to lean fish. The level of n-6 fatty acids is about 4-fold higher than in 2006.

VKM has estimated the contribution from fish to the recommended daily intakes of certain nutrients. Fish is the major source of EPA+DPA+DHA, but for vitamin D, iodine and selenium, other sources in addition to fish are needed in order to meet the recommendation. Fish is not a major dietary source of n-6 fatty acids. The contribution of dietary n-6 fatty acids from farmed salmon compared to the overall dietary intake of n-6 fatty acids is low (less than 3%).

VKM concludes that with current average consumption of fish, the contribution of **EPA and DHA** from fish will reach the European recommended intake of EPA+DHA for adults and 2-year-olds. For pregnant women the average EPA+DHA intake is insufficient to meet the European recommendation for this group. However, the average intake of DHA is sufficient to meet the national intake recommendation for pregnant women.

For **vitamin D**, current average fish consumption contributes approximately 20% of the national recommended intakes for adults but less for pregnant women and 2-year-olds.

Furthermore, with current average fish consumption, low intakes of **selenium and iodine** from fish relative to the national recommended values may be complemented by intake from other dietary sources.

VKM has made various scenarios to foresee how possible changes in fish consumption pattern and amounts will affect the contribution from fish to recommended intakes of specific important nutrients. According to the scenarios, increasing the consumption of fatty fish will increase the intakes particularly of vitamin D, EPA+DPA+DHA, while increasing consumption of lean fish will increase the intakes particularly of iodine. Furthermore, VKM notes that the choice of fatty fish species, e.g. farmed Atlantic salmon, mackerel and herring is also of importance for nutrient intake due to differences in nutrient content.

Risk characterisation of undesirable substances in fish

The available concentration data of contaminants in wild fish is not suitable for time-trend analyses. A rough comparison of contaminant concentrations between 2006 and 2014 indicates minor or no changes in concentrations of mercury, dioxins and dl-PCBs in wild fish species. However, for dioxins and dl-PCBs, a decreasing environmental time-trend is expected to be reflected also in wild fish species.

Due to replacement of fish oil and fish protein with plant proteins and vegetable oils in farmed fish feed, the concentrations of dioxins and dioxin-like PCBs, and mercury have changed in farmed Atlantic salmon. VKM concludes that the current concentrations of dioxins and dl-PCBs, and mercury in farmed Atlantic salmon are reduced to about 30 and 50%, respectively, of the corresponding levels in 2006.

VKM has estimated the dietary exposure to contaminants from fish based on mean levels in different fish species and compared the exposure levels with the relevant health based guidance levels, tolerable weekly intakes (TWIs). A tolerable intake is the amount of a

substance, or substance group, which can be consumed safely throughout a person's lifetime without appreciable risk of adverse health effects. Tolerable intakes incorporate safety margins, in order to protect all parts of the population.

VKM concludes that with the present mean concentration of **mercury** in fish on the Norwegian market and the present fish consumption in Norway, the methylmercury exposure from fish is below the tolerable weekly intake (TWI) of 1.3 µg/kg bw/week for more than 95% of the population of 2-year-olds, adults and pregnant women. This exposure represents a negligible risk and is of no concern.

With the present mean level of **dioxins and dl-PCBs** in fish on the Norwegian market and the present fish consumption in Norway, high fish consumption (the 95th percentile) contributes with up to 50%, 19%, 67% of the TWI of 14 pg TEQ/kg bw/week for adults, pregnant women and 2-year-olds respectively. Daily consumption of cod liver oil or fish oil (which is common in all population groups) in amounts as suggested on the product will in addition contribute with 0.8 to 16% of the TWI, depending on the body weight. With the present TWI and taking into consideration that fish and fish products are significant sources to dioxins and dl-PCBs in the Norwegian diet, VKM concludes that the exposure from fish to dioxins and dl-PCBs represents negligible risk and is of no concern.

VKM is of the opinion that the present exposure to **residues** of veterinary medicinal products **including residues of antibiotics** in farmed fish in the Norwegian diet is of no concern since the levels are very low and often not detectable even with sensitive analytical methods.

For new contaminants in fish feed like the **pesticide endosulfan, polyaromatic hydrocarbon (PAHs) and mycotoxins**, VKM is of the opinion that the concentrations in farmed fish in the Norwegian diet are likely not a food safety issue since the concentrations are very low and often not detectable even with sensitive analytical methods.

Regarding the environmental contaminants brominated flame retardants, VKM refers to the conclusions in a risk assessment from EFSA in 2011 that the health risk associated with the current exposure to these compounds is low. The amount of fluorinated compounds such as PFOS and PFOA in the Norwegian diet is much lower than what is tolerable according to an EFSA assessment in 2008.

VKM has made various scenarios to foresee how possible changes in fish consumption pattern and amounts will affect the exposure from fish to TWIs of methylmercury, and dioxins and dl-PCBs. Fish is the only source for methylmercury exposure from foods, whereas exposure to dioxins and dl-PCBs also comes from other foods than fish. Based on these scenarios, where only exposure to dioxins and dl-PCBs from fish were taken into consideration, VKM is of the opinion that fish consumption in line with the food-based dietary guideline of 300-450 g fish, hereof 200 g fatty fish per week, does not lead to exposures to dioxins and dl-PCBs or methylmercury from either fatty or lean fish exceeding the respective TWIs, and is therefore, from a contaminant exposure perspective, of no concern.

However, since there are other food sources in the Norwegian diet that contribute to exposure to these contaminants, VKM performed a simple model estimate of weekly intake of dioxins and dl-PCBs in adults from various amounts of farmed salmon and other foods. Based on this scenario, VKM is of the opinion that there is negligible risk associated with eating farmed Atlantic salmon with the present mean concentrations of dioxins and dl-PCBs. The TWI is not exceeded when consuming amounts equivalent to 1400 g farmed salmon weekly for adults (representing 9 weekly dinner servings). Neither is the TWI exceeded when exposures to dioxins and dl-PCBs from other foods and cod liver oil are taken into consideration. In comparison, an adult can consume about 800 g mackerel weekly (representing 5 weekly dinner servings) with current mean concentration of dioxins and dl-PCBs without exceeding TWI. From a contaminant exposure perspective consumption of farmed salmon is of no concern. This also applies for commercially available wild caught fish like mackerel.

Benefit – risk comparison

Following a comprehensive assessment of the scientific literature on the positive health effects of fish consumption and the contribution from fish to intake of beneficial compounds as well as exposure to hazardous contaminants in Norway, VKM concludes that the benefits clearly outweighs the negligible risk presented by current levels of contaminants and other known undesirable substances in fish. Furthermore, adults including pregnant women with fish consumption less than one serving per week may miss the beneficial effects on cardiovascular diseases and optimal neurodevelopment in the foetuses and infants. In contrast to the conclusion in 2006, VKM concludes that there is no reason for specific dietary limitations on fatty fish consumption for pregnant women.

Uncertainties

This benefit-risk assessment is composed of several different parts. Various databases are used, including data on levels of nutrients and contaminants in fish feed and fish which may all contain uncertainties which in turn may influence the overall assessment. Furthermore, there may be uncertainties in the estimated fish consumption data retrieved from the dietary food surveys and there may be weaknesses in the epidemiological studies about health effects of fish consumption. Despite some limitations in assessing the fish consumption and the uncertainties related to the estimated intakes of nutrients and exposures to contaminants from fish and fish products, VKM concludes that the intake and exposure estimates presented in this opinion are within realistic ranges for each study population. VKM compared intakes of nutrients with national recommended intake values and exposures to contaminants with internationally recognised health based guidance values (tolerable intakes). Likewise, the benefits for health associated with fish consumption were also evaluated by international bodies, and the uncertainties in these assessments were not evaluated by VKM. VKM considers the overall uncertainty in the outcome of the present assessment on benefit and risk of fish consumption in Norway to be low.

Key words: VKM, benefit-risk assessment, fish, fish feed, farmed Atlantic salmon, fish consumption, health effects, nutrients in fish, marine n-3 fatty acids, iodine, vitamin D, selenium, contaminants in fish, dioxins and dl-PCBs, mercury, Norwegian Scientific Committee for Food Safety.

Sammendrag

Oppdrag fra Mattilsynet

I september 2013 ba Mattilsynet Vitenskapskomiteen for mattrygghet (VKM) om å oppdatere relevante deler av nytte-risikovurderingen av fisk i norsk kosthold utgitt av VKM i 2006. Bakgrunnen for oppdraget var ny kunnskap og data om innhold av enkelte næringsstoffer og fremmedstoffer både for villfisk og oppdrettsfisk siden 2006. Andelen vegetabiliske ingredienser som brukes i fôr til oppdrettsfisk har økt i de senere årene og nye nasjonale kostholdsundersøkelser for voksne og barn har blitt gjennomført.

Mattilsynet viste i sitt oppdrag til VKM rapporten fra 2006, som påpekte at den positive helseeffekten av å spise fisk spesielt var relatert til fiskens innhold av flerumettede fettsyrer og vitamin D. VKM konkluderte den gang med at forurensninger som kan utgjøre en potensiell risiko for folkehelsen gjennom konsum av fisk hovedsakelig var metylkvikksølv, dioksiner og dioksinlignende PCB.

Mattilsynets bestilling omfattet en revurdering av fiskekonsumet i Norge med fokus på spesifikke næringsstoffer; n-3-fettsyrer (eikosapentaensyre (EPA), dokosapentaensyre (DPA), dokosaheksaensyre (DHA)), vitamin D, og mineralene jod og selen, og på bestemte forurensninger; kvikksølv, dioksiner og dioksinlignende PCB (dl-PCB). VKM ble bedt om å vurdere de viktigste endringene i bruken av råvarer i fôr til oppdrettsfisk, og hvordan disse igjen påvirker nivåene av næringsstoffer, kvikksølv, dioksiner og dioksinlignende PCB i fiskefôret. Videre ble VKM bedt om å vurdere i hvilken grad nivåene av næringsstoffer og forurensninger i fisk har endret seg siden 2006, samt beskrive endringene og beregne inntak av de aktuelle stoffene ut i fra nasjonale kostholdsundersøkelser. VKM ble også bedt om å vurdere fordelene ved å spise fisk med hensyn til inntak av næringsstoffer opp mot risikoen forbundet med inntak av kvikksølv, dioksiner og dioksinlignende PCB og vurdere om dette endrer konklusjonene fra rapporten i 2006. I tillegg, på bakgrunn av oppdatert kunnskap, ble VKM bedt om å kommentere om andre stoffer, som plantevernmidler- og medisinrester, kan påvirke konklusjonene med hensyn til innvirkning på folkehelsen.

Mattilsynet og Helsedirektoratet vil bruke den oppdaterte vurderingen som grunnlag for offentlige anbefalinger om konsum av fisk og fiskeprodukter.

Hvordan VKM har arbeidet med og besvart Mattilsynets bestilling

VKM nedsatte en arbeidsgruppe som besto både av VKM medlemmer og eksterne eksperter for å svare på bestillingen. Underveis i arbeidet hadde flere av VKMs vitenskapelige faggrupper rapporten til gjennomsyn og kommentering. VKMs Hovedkomite har i flere møter behandlet rapporten og gitt den sin endelige godkjenning.

VKM har i sin vurdering hovedsakelig brukt forekomsttall både for næringsstoffer og miljøgifter i fiskefôr, oppdrettsfisk og villfisk fra nasjonale kontroll- og overvåkingsprogrammer, men forekomsttall har også blitt hentet fra fagfelleverderte artikler.

VKM har estimert fiskekonsumet i tre grupper av befolkningen (2 år gamle barn, voksne og gravide kvinner). Det estimerte fiskekonsumet ble så sammenlignet med nasjonale kostråd for fiskekonsum.

For å vurdere helseeffekter av fiskekonsumet, ble dagens estimerte fiskekonsum også sammenlignet med resultater fra vurderinger gjort av anerkjente internasjonale organisasjoner og resultater fra epidemiologiske studier som har sett på mulige sammenhenger mellom fiskekonsum og spesifikke helseutfall. Det ble utført litteratursøk for å identifisere relevante epidemiologiske studier. VKM har ikke systematisk vurdert oversiktsartikler, metaanalyser eller enkeltstudier med hensyn på vektning av holdepunkter, men har oppsummert resultatene fra studiene funnet i litteratursøket. En vurdering av de enkelte studiene som inngikk i oversiktsartiklene eller metaanalysene ble ansett å ligge utenfor rammen av denne rapporten.

I tillegg ble inntak av næringsstoffer og eksponering for miljøgifter fra fisk estimert basert på dagens fiskekonsum i de ulike befolkningsgruppene. For nyttekarakterisering av de spesifikke næringsstoffene ble det estimerte inntaket av næringsstoffer sammenlignet med nasjonale anbefalinger for inntak av de respektive stoffene. For summen av EPA og DHA ble det også gjort en sammenligning med europeiske anbefalinger for inntak. For risikokarakterisering av miljøgifteksponering fra fisk benyttet VKM helsebaserte referanseverdier satt av internasjonale risikovurderingsorganer (WHO, EFSA).

VKM tok til følge at Mattilsynet ønsket en vurdering av fisk, mens VKM rapporten i 2006 omfattet både fisk og annen sjømat.

VKM har lagt vekt på de spesifikke næringsstoffene og miljøgiftene som Mattilsynet ba om. I tillegg har VKM omtalt andre stoffer som kan ha betydning for vurdering av risiko, slik som legemiddelrester, inkludert rester av antibiotika, nye miljøgifter i fiskefôr, som plantevernmiddelet endosulfan, polysykliske aromatiske hydrokarboner, mykotoksiner, syntetiske antioksidanter som ethoxyquin, butylhydroksyanisol (BHA) og butylhydroksytoluen (BHT), samt noen miljøgifter i gruppene av bromerte flammehemmere og perfluorerte organiske forbindelser.

Bakgrunn

Fisk en viktig kilde til godt balansert kosthold med hensyn til protein og viktige næringsstoffer som EPA og DHA, vitamin D, jod og selen. På den annen side er fisken også en kilde til eksponering for miljøgifter som dioksiner, PCB og kvikksølv.

I løpet av de siste 10 årene har det vært en stor forandring i råvarer som brukes i fiskefôr, og i 2013 besto 70 % av fôret av terrestriske planteproteiner og planteoljer. Endringene i konsentrasjoner av næringsstoffer og fremmedstoffer i fôr til oppdrettslaks og oppdrettsørret gjenspeiles i endret konsentrasjon og sammensetning av de samme næringsstoffene og fremmedstoffene i fisken.

Dagens nasjonale kostråd er å spise fisk til middag 2-3 ganger per uke i alle aldersgrupper. Dette representerer 300-450 g fisk per uke for voksne, inkludert minst 200 g fet fisk, som laks, ørret, makrell og sild. Fisk er også anbefalt som pålegg. Videre anbefales et daglig tilskudd av vitamin D til spedbarn fra fire ukers alder, og hvis dette tillegget er tran, vil det i tillegg sikre tilstrekkelig inntak av EPA og DHA.

Denne nytte-risikovurderingen består av tre deler, dvs. en nyttevurdering, en risikovurdering og en sammenligning av nytten og risikoen. Metodikken er i samsvar med veiledning fra EFSA (EFSA, 2012).

Fiskekonsum i Norge sammenlignet med nasjonale kostholdsråd

VKM har brukt informasjon om fiskekonsum fra nyere nasjonale kostholdsundersøkelser blant 2-åringer (Småbarnskost 2007) og voksne 18-70 år (Norkost 3, 2010/2011), samt informasjon fra gravide kvinner som har besvart matvarefrekvensskjemaet i den norske mor og barn-undersøkelsen (MoBa, 2002-2008). Den nasjonale kostholdsundersøkelsen Ungkost 2000, som omfatter aldersgruppene 4-, 9- og 13-åringer, ble ansett for gammel til å bli brukt. Det er derfor ikke kjent om mønsteret i fiskekonsumet har endret seg for disse aldersgruppene, verken når det gjelder mengde eller type fisk som konsumeres.

Selv om det er metodiske forskjeller mellom kostholdsundersøkelsene som ble brukt i 2006 og 2014, er mengden fisk konsumert stort sett uforandret i de ulike aldersgruppene. Fordelingen mellom fet og mager fisk er også stort sett uforandret; ca. 60 % mager og 40 % fet fisk av det totale fiskekonsumet.

Gitt en porsjonsstørrelse på 150 g fisk tilsvarer fiskekonsumet hos en gjennomsnittlig voksen 2-3 fiskemiddager i uken og hos en gjennomsnittlig gravid kvinne 1-2 fiskemiddager per uke. En to-åring fiskekonsum tilsvarer 1-2 middager per uke gitt en porsjonsstørrelse på 75 g. Tabellen nedenfor beskriver fiskeinntak i de utvalgte gruppene.

Gjennomsnittlig ukentlig fiskekonsum i gram (g) (uttrykt som rå fisk) hos 2-åringer (Småbarnskost 2007, n=1674), voksne (Norkost 3, n=1787) og gravide kvinner (MoBa, n=86277)

Befolkningsgrupper	Gjennomsnittlig fiskekonsum g/uke			Fiskerogn og fiskelever
	Fisk, totalt	Mager fisk (≤ 5 % fett)	Fet fisk (> 5 % fett)	
2-åringer	112	70	35	7
Voksne	364	210	147	7
Gravide kvinner	217	126	77	14

VKM konkluderer med at av de ulike befolkningsgrupper, er det kun voksne (18-70 år) med et gjennomsnittlig eller høyere konsum av fisk som når de nasjonale matvarebaserte kostrådene for total fiskekonsum. Gjennomsnittlig totalt fiskekonsum og konsum av fet fisk hos barn (2-åringer) og gravide kvinner, så vel som konsum av fet fisk hos voksne, er lavere enn anbefalt. Fiskekonsumet hos gravide kvinner og to-åringer er for lavt til å nå anbefalt mengde i forhold til de matvarebaserte kostrådene.

Helseeffekter av fiskekonsum

VKM mener at i henhold til epidemiologiske studier er nettoeffekt av det nåværende, gjennomsnittlige konsumet av fisk hos norske voksne, inkludert gravide kvinner, gunstig for å forebygge spesifikke hjerte-karsykdommer (spesielt dødelighet på grunn av hjertesykdom, men også med hensyn til iskemisk hjerneslag, ikke-fatale hendelser av koronar hjertesykdom, hjertesvikt og atrieflimmer), samt for optimal utvikling av nervesystemet hos foster og spedbarn. Videre mener VKM at de som har fiskekonsum som er lavere enn tilsvarende én middagsporsjon per uke vil gå glipp av de gunstige virkningene av fiskekonsum på hjerte- og karsykdommer og optimal nevrologisk utvikling hos foster og spedbarn.

Helsefordelene ved fiskespising opptrer fra 1-2 måltider per uke og opp til 3-4 måltider per uke. Det kan ikke trekkes sikre slutninger om nytte og risiko av enda høyere fiskekonsum, fordi det er for få som spiser mer enn 3-4 måltider per uke i de epidemiologiske studiene. Det trengs også mer kunnskap om hvorfor fisk er helsebringende.

Nyttekarakterisering av næringsstoffer fra fisk

VKM mener at det har vært liten eller ingen endringer i sammensetning og konsentrasjoner av næringsstoffer i villfanget fisk siden 2006

Fordi fiskeolje og fiskeprotein er erstattet med planteproteiner og planteoljer i fôret til oppdrettsfisk, er konsentrasjonene av EPA, DPA og DHA i oppdrettslaks ca. 50 %, og selen ca. 40 % av nivåene i 2006, mens konsentrasjonen av vitamin D ser ut til å være uendret. Nivået av jod i oppdrettslaks var lavt i 2006, og er fortsatt lavt sammenlignet med mager fisk. Nivået av n-6 fettsyrer er omtrent fire ganger høyere enn i 2006.

VKM har beregnet bidraget fra fisk til det anbefalte daglige inntaket av bestemte næringsstoffer. Fisk er hovedkilden til EPA+DPA+DHA, mens for vitamin D, jod og selen er andre kilder i tillegg til fisk nødvendig for å oppnå anbefalt inntak. Fisk er ikke en viktig kilde for n-6 fettsyrer. Oppdrettslaks bidrar i liten grad (mindre enn 3 %) til inntak av n-6 fettsyrer i forhold til det samlede inntaket av n-6 fettsyrer fra kosten.

VKM konkluderer at med dagens gjennomsnittlige konsum av fisk er bidraget av **EPA og DHA** fra fisk hos voksne og 2-åringer i tråd med europeiske anbefalte inntak av EPA+DHA. For gravide kvinner er det gjennomsnittlige EPA+DHA-inntaket ikke tilstrekkelig til å dekke den europeiske anbefalingen for gravide. Imidlertid imøtekommer det gjennomsnittlig inntaket av DHA hos gravide kvinner det nasjonalt anbefalte inntak for gravide.

Dagens gjennomsnittlige konsum av fisk bidrar med ca. 20 % av det nasjonalt anbefalte inntaket for **vitamin D** hos voksne, mens bidraget fra fisken er lavere for gravide kvinner og 2-åringer.

Dagens gjennomsnittlige konsum av fisk bidrar i begrenset grad til inntak av **selen og jod** i forhold til nasjonalt anbefalte inntak. Annen mat bidrar til inntak av disse stoffene.

VKM har laget ulike scenarier for å forutse hvordan eventuelle endringer i mønster av fiskekonsum og mengde fisk vil kunne påvirke bidraget fra fisk til anbefalte inntak av spesifikke, viktige næringsstoffer. Ifølge scenariene vil økt konsum av fet fisk gi økt inntak særlig av vitamin D, EPA+DPA+DHA, mens økt konsum av mager fisk vil gi økt inntak særlig av jod. VKM påpeker at valg av type fet fisk også vil ha betydning for næringsinntaket fordi ulike fiskeslag, f.eks. oppdrettslaks, makrell og sild, har ulikt næringsinnhold.

Risikokarakterisering av uønskete forbindelser i fisk

Tilgjengelige tall for konsentrasjoner av miljøgifter i villfisk er ikke egnet for tidstrendanalyser. En grov sammenligning av miljøgiftnivåer i 2006 og 2014 indikerer små eller ingen endringer av kvikksølv, dioksiner og dl-PCB i villfisk. Imidlertid viser forekomsten av dioksiner og dl-PCB i miljøet en generelt nedadgående tidstrend, og denne nedgangen er forventet å bli reflektert også i villfisk.

Fordi fiskeolje og fiskeprotein i stor grad er erstattet med plante proteiner og planteoljer i fiskefôret, er konsentrasjonene av dioksiner og dl-PCB og kvikksølv endret i oppdrettsfisk. VKM konkluderer med at dagens konsentrasjoner av dioksiner og dioksinlike PCB og kvikksølv i oppdrettslaks er redusert til henholdsvis ca. 30 % og 50 % av nivåene i 2006.

VKM har beregnet eksponeringen for miljøgifter fra fiskekonsum basert på gjennomsnittsnivåer i ulike fiskearter og sammenlignet eksponeringsnivåer med relevante helsebaserte referanseverdier, tolerable ukentlige inntak (Tolerable Weekly Intake - TWI). Et tolerabelt inntak er den mengden av et stoff, eller stoffgruppe, som kan inntas trygt gjennom hele livet uten nevneverdig risiko for uheldige helseeffekter. Tolerable inntak innehar sikkerhetsmarginer for å beskytte alle deler av befolkningen.

VKM konkluderer med at med dagens gjennomsnittlige nivå av kvikksølv i fisk på det norske markedet, og det nåværende fiskekonsumet i Norge, er eksponeringen for metylkvikksølv fra fisk under det tolerable ukentlige inntaket på 1,3 mikrogram/kg kroppsvekt/uke for mer enn 95 % av to-åringer, voksne og gravide kvinner. Denne eksponeringen representerer en ubetydelig risiko som ikke fører til bekymring.

Med dagens gjennomsnittlige nivå av **dioksiner og dl-PCB** i fisk på det norske markedet, og det nåværende fiskekonsumet i Norge, bidrar høyt konsum av fisk (95-persentilen) med opp til 50 % hos voksne, 19 % hos gravide og 67 % hos 2-åringer av tolerabelt ukeinntak på 14 pg TEQ/kg kroppsvekt/uke. Daglig inntak av tran eller fiskeoljer (som er vanlig i alle grupper av befolkningen) i mengder som foreslått på produktet, vil i tillegg bidra med 0,8 % til 16 % av tolerabelt ukeinntak avhengig av kroppsvekt. Fisk og fiskeprodukter er vesentlige kilder til dioksiner og dl-PCB i norsk kosthold. VKM konkluderer likevel med at med gjeldende tolerabelt ukeinntak, så representerer dagens eksponering for dioksiner og dl-PCB fra fisk en ubetydelig risiko som ikke fører til bekymring.

VKM mener at den nåværende eksponeringen for **legemiddelrester inklusive rester av antibiotika** i oppdrettsfisk ikke fører til bekymring siden nivåene er svært lave og ofte ikke gjenfinnes selv med følsomme analysemetoder.

For nye miljøgifter i fiskefôr som plantevernmiddelet endosulfan, polyaromatiske hydrokarboner (PAH) og soppgifter (mykotoksiner), er VKM av den oppfatning at konsentrasjonene i oppdrettsfisk i norsk kosthold trolig ikke utgjør noe mattrygghetsproblem siden konsentrasjonene er svært lave og ofte ikke gjenfinnes selv med følsomme analysemetoder.

Når det gjelder miljøgiftene bromerte flammehemmere viser VKM til EFSA, som i 2011 konkluderte at helse risikoen knyttet til nåværende eksponering for disse stoffene er lav. Mengdene perfluoreerte forbindelser som PFOS og PFOA i norsk kosthold er mye lavere enn det som er tolerabelt i henhold til en risikovurdering fra EFSA i 2008.

VKM har laget ulike scenarier for å kunne forutse hvordan eventuelle endringer i fiskekonsum vil påvirke bidraget fra fisk til det tolerable ukeinntaket for henholdsvis metylkvikksølv, og dioksiner og dioksinlike PCB. Fisk er eneste kilde til metylkvikksølv eksponering fra mat, mens for dioksiner og dioksinlike PCB bidrar annen mat også til eksponeringen. Basert på disse scenariene mener VKM at et fiskekonsum blant voksne i tråd med nasjonale matvarebaserte kostråd, 300-450 g fisk herav 200 g fet fisk per uke, ikke bidrar med dioksiner og dioksinlike PCB eller metylkvikksølv, verken fra fet eller mager fisk, i mengder som overskrider de respektive tolerable ukeinntakene. Denne eksponeringen utgjør derfor ingen bekymring fra et miljøgifteksponeringsperspektiv.

Siden flere andre matvarer i det norske kostholdet bidrar til eksponeringen for dioksiner og dl-PCB, gjorde VKM et enkelt modellestimat av ukentlig eksponering for dioksiner og dioksinlike PCB fra ulike mengder oppdrettslaks og andre matvarer hos voksne. Basert på dette scenariet mener VKM at med dagens gjennomsnittlige konsentrasjon av dioksiner og

dioksinlike PCB er det ubetydelig risiko forbundet med å spise oppdrettslaks. Det tolerable ukeinntaket overskrides ikke selv ved konsum av mengder som tilsvarer 1400 g ukentlig for voksne (tilsvarende ni ukentlige middagsporsjoner). Det tolerable ukeinntaket overskrides heller ikke når eksponering for dioksiner og dl-PCB fra andre matvarer og tran blir tatt hensyn til. Til sammenligning kan en voksen konsumere ca. 800 g makrell i uken (fem ukentlige middagsporsjoner) med den nåværende gjennomsnittlige konsentrasjon av dioksiner og dioksinlike PCB uten at det tolerable ukeinntaket overskrides. I perspektiv av miljøgiftinnholdet kan oppdrettsfisk spises uten bekymring. Det samme gjelder for kommersielt tilgjengelig villfisk som makrell.

Nytte - risiko sammenligning

Etter en helhetlig vurdering av den vitenskapelige litteraturen om de positive helseeffektene av fiskekonsum og bidraget fra fisk til inntak av viktige næringsstoffer samt eksponering for farlige miljøgifter i Norge, konkluderer VKM med at fordelene klart oppveier den ubetydelige risikoen som dagens nivå av forurensninger og andre kjente fremmedstoffer i fisk representerer. Videre er det mulig at voksne inklusive gravide kvinner med fiskekonsum mindre enn tilsvarende en ukentlig middagsporsjon, går glipp av gunstige effekter på hjertekarsykdommer og optimal utvikling av nervesystemet hos foster og spedbarn. I motsetning til konklusjonen i 2006, konkluderer VKM nå med at det ikke er grunn til spesifikke kostråd for gravide om begrensninger på konsum av fet fisk.

Usikkerhet

Denne nytte-risikovurderingen er sammensatt av flere ulike deler. Forskjellige databaser er brukt, inkludert data på nivåene av næringsstoffer og fremmedstoffer i fiskefôr og fisk, og alle kan inneholde usikkerheter som igjen kan påvirke den samlede vurderingen. Videre kan det være usikkerhet i fiskekonsumet som er estimert ut i fra de nasjonale kostholdsundersøkelsene, og det kan være svakheter i epidemiologiske studier om helseeffektene av fiskekonsum. Til tross for noen begrensninger i vurderingen av fiskekonsum og usikkerhetene knyttet til de estimerte inntakene av næringsstoffer og eksponeringene for forurensninger fra fisk og fiskeprodukter, konkluderer VKM at de inntaks- og eksponeringsestimatene som presenteres i denne rapporten er realistiske for hver av alderspopulasjonene. VKM sammenlignet inntak av næringsstoffer med nasjonale anbefalte inntaksverdier og eksponering for forurensninger med internasjonalt anerkjente helsebaserte referanseverdier (tolerabelt inntak). Likeledes er helsegevinstene forbundet med konsum av fisk også evaluert av internasjonale organer, men usikkerheten i disse vurderingene ble ikke vurdert av VKM. VKM anser at den generelle usikkerheten i utfallet av denne nytte-risikovurderingen av fiskekonsumet i Norge er lav.

Nøkkelord: VKM, nytte-risikovurdering, fisk, fiskefôr, oppdrettslaks, fiskekonsum, helseeffekter, næringsstoffer i fisk, marine n-3 fettsyrer, jod, vitamin D, selen, forurensninger i fisk, dioksiner og dioksinlike PCB, kvikksølv, Vitenskapskomiteen for mattrygghet.

Abbreviations and glossary

Abbreviations

95 th perc.	95 th percentile
AA	arachidonic acid
AAP	American Academy of Pediatrics
ACS	acute coronary syndrome
ADI	acceptable daily intake
AF	atrial fibrillation
AFSSA/ANSES	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail/French Agency for Food, Environmental and Occupational Health & Safety
AI	adequate intake
ALA	alpha linolenic acid
ao	among others
AR	average requirement
BHA	butylhydroksyanisol
BHT	butylhydroksytoluen
BMD	benchmark dose
BMDL	benchmark dose lower confidence limit
bw	body weight
Ca	chemical symbol for calcium
CEN	European Committee for Standardization
CHD	coronary heart disease
CI	confidence interval
CNS	central nervous system
CONTAM	EFSA Panel on Contaminants in the Food Chain
COT-	Committee on Toxicity, UK
CRL	community reference laboratories
DALY	disability-adjusted life year
DDD	dichlorodiphenyldichloroethane (breakdown product of DDT)
DDE	dichlorodiphenyldichloroethylene (breakdown product of DDT)
DEHP	di-2-ethylhexyl phthalate
DDT	dichlorodiphenyltrichloroethane (an organochlorine pesticide)
DHA	docosahexaenoic acid
DiBP	di-isobutyl phthalate
dl-PCBs	dioxin-like PCBs
DPA	docosapentaenoic acid
EER	estimated energy requirement
EFSA	European Food Safety Authority
EPA	eicosapentaenoic acid
EQ	ethoxyquin

FFQ	food frequency questionnaire
HBCD	hexabromocyclododecane
HBCDD	hexabromocyclododecane
HCH	hexachlorocyclohexane
HCB	hexachlorobenzene
HF	heart failure
Hg	chemical symbol for mercury
IQ	Intelligence Quotient
IOM	Institute of Medicine (US)
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
KBS	Norwegian software system used to calculate dietary intake of nutrients
kg	kilogram
LB	lower bound
LA	linoleic acid
LCPUFA	long chain polyunsaturated fatty acid
LI	lower intake
LOD	limit of detection
LOAEL	Lowest Observable Adverse Effect Level
LOEL	Lowest Observable Effect Level
LOQ	limit of quantification
MI	myocardial infarction
MJ	mega joule
ML	maximum level
MoBa	Norwegian Mother and Child Cohort Study
MoBa Val	MoBa Validation Study
MOE	margin of exposure
MRL	maximum residue level
MRPL	minimum required performance limits
ng	nanogram
NRL	national reference laboratories
ndl-PCBs	non-dioxin-like PCBs
NOAEL	No Observed Adverse Effect Level
NMKL	Nordisk metodikkomité for næringsmidler (i.e. Nordic Methodological Committee for Food)
NNR5	Nordic Nutrition Recommendations 5 th edition
NPN	non-protein nitrogen
P95	95 th percentile
PBDEs	polybrominated diphenyl ethers
PBPK	physiologically based pharmacokinetic modelling
PCBs	polychlorinated biphenyls
PCDDs	polychlorinated dibenzodioxins
PCDFs	polychlorinated dibenzofurans
PDI	Psychomotor Development Index

pers. comm.	personal communication
PFAS	perfluoroalkylated substance
PFOS	perfluorooctanosulfonate
PFOA	perfluorooctanoic acid
PG	propylgallate
pg	picogram
PICO	Population Intervention Comparison Outcome
POPs	persistent organic pollutants
prep.	preparation
PTDI	provisional tolerable daily intake
PTWI	provisional tolerable weekly intake
PUFA	polyunsaturated fatty acid
QALY	The quality-adjusted life year
RCT	randomized control trials
RR	relative risk
SCF	Scientific Committee for Food; now replaced by EFSA
SD	standard deviation
T2DM	type-2 diabetes mellitus
TBBPA	tetrabromobisphenol A
TOR	terms of reference
TCDD	tetrachlorodibenzo(p)dioxin
TDI	tolerable daily intake
TE	toxic equivalent
TEF	TCDD toxic equivalency factor
TEQ	sum of TCDD toxic equivalents (concentration of each dioxins, furan and dl-PCBs multiplied with its corresponding TEF value and then summarised)
TWI	tolerable weekly intake
UB	upper bound
UL	Upper intake levels (see Glossary for definition)
US	United States
US ATSDR	United States Agency for Toxic Substances and Disease Registry
VKM	Norwegian Scientific Committee for Food Safety
VT	venous thromboembolism
VMP	veterinary medicinal product
WHO	World Health Organization
ww	wet weight

Glossary

Average requirement (AR) is the daily intake of a specific nutrient estimated to meet the requirement in 50% of healthy people in an age- and gender-specific group.

Acceptable daily intake (ADI) is the amount of an additive or a pesticide residue in food that a person can ingest daily throughout life without an appreciable health risk.

Benchmark dose (BMD) is a dose or concentration that produces a predetermined change in response rate of an adverse effect (called the benchmark response or BMR) compared to background. The BMD approach estimates the dose that causes a low but measurable target organ effect.

Body burden is the total amount of a particular chemical present in the body.

Benchmark dose lower confidence limit (BMDL) is a statistical lower confidence limit on the dose producing a predetermined level of change in adverse response compared with the response in unexposed individuals.

Cocktail effect is a popular term of combined toxic effect of multiple chemical exposures.

“Consumers only” is a term that refers to a calculated value based on data from only those who reported consumption of the specific food item.

Disability-adjusted life year (DALY) is a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death.

Frequent consumption is a relative quantification related to a study dependent scale.

High consumers are defined by the 95th percentile.

Lower bound values are values below limit of detection (LOD) or limit of quantification (LOQ) and are thus set to zero.

Lower intake (LI) is a limit below which long-term intake are associated with an increased risk of developing deficiency symptoms.

Maximum residue limit (MRL) of a veterinary medicinal product is the maximum acceptable concentration of a substance that may be found in a food product obtained from an animal that has received a veterinary medicine. The MRL for an active substance is based on its pharmacological and toxicological data which are derived from experimental animal studies. The EU-Commission approves the MRL values, which are implemented in Norway by the Norwegian Food Safety Authority.

Maximum residue level (MRL) of a pesticide refers to the upper allowed level of residues of a particular pesticide that may remain in crops on the market, e.g. in feed or food, based on Good Agricultural Practice (GAP).

Medium bound is when values below limit of detection (LOD) or limit of quantification (LOQ) are set to half of the LOD or LOQ.

n-3 polyunsaturated fatty acids (PUFAs) refer to the fatty acids eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), docosahexaenoic acid (DHA), and alpha linolenic acid (ALA).

n-3 long-chain polyunsaturated fatty acids (LCPUFAs) refer to the long-chain fatty acids EPA, DPA and DHA only (not ALA).

Polychlorinated biphenyls (PCBs) consist of 209 different congeners, amongst which the congeners numbered 121, 153 and 180 are the most commonly analysed for.

Quality-adjusted life year (QALY) is a measure of disease burden, including both the quality and the quantity of life lived.

The Stockholm Convention on Persistent Organic Pollutants (POPs) is a global treaty administered by the United Nations Environment Programme (UNEP) to protect human health and the environment from chemicals, and first entered into force in 2004 (Stockholm Convention on POPs 2004 <http://www.chm.pops.int>). The criteria for being included in SC are persistence, bioaccumulation, potential for long-range transport and adverse effects.

Tolerable weekly intake (TWI) is the amount of a substance, or substance group, which can be consumed per week safely throughout a person's lifetime without appreciable risk of adverse health effects.

Upper bound is when values below limit of detection (LOD) or limit of quantification (LOQ) are set equal to the LOD or LOQ.

Upper intake levels (UL) are maximum levels of daily chronic intakes judged to be unlikely to pose a risk of adverse health effects in humans.

Withdrawal times for veterinary medicinal products (VMPs) are based on the Maximum Residue Limit (MRL) of the active substance and results from analyses of residue concentrations in the tissue and species in question, and decided by the Norwegian Medicinal Agency.

Background as provided by the Norwegian Food Safety Authority

Fish and fish products contain substances that are beneficial to health as well as contaminants and other unwanted substances. Environmental contaminants are found in varying degrees in different types of food, and fish can be one of the sources of these substances in our diet. In 2004, the Norwegian Food Safety Authority requested the Norwegian Scientific Committee for Food Safety (VKM) to conduct a comprehensive assessment of fish and other seafood. The assessment was to take into account both the nutritional benefits of fish consumption and the health risks associated with the exposure to contaminants and other undesirable substances.

In 2006, VKM published the report "A comprehensive assessment of fish and seafood in the Norwegian diet." The report stated that compared to many other countries, the consumption of fish and other types of seafood in Norway was high. Two thirds of the fish consumption comprised lean fish and minced fish products, and about one third was fatty fish. While most adults ate some fish and other seafood, a high percentage of children and teenagers did not eat such food at all. Young women consumed less fish than the general population.

Since 2006, new knowledge about the content of some nutrients and contaminants in fish feed, fish and fish products has become available, both in wild and farmed fish. In recent years, the proportion of vegetable ingredients used in fish feed has increased. Moreover, results from new national dietary surveys for adults and children are available. In view of the increased knowledge, the Norwegian Food Safety Authority requests VKM to update relevant parts of the benefit-risk assessment of fish in the Norwegian diet. The Norwegian Food Safety Authority and the Norwegian Directorate of Health will use the updated assessment as a basis for public recommendations concerning the consumption of fish and fish products. In 2006, VKM pointed out that the positive impact of fish consumption on public health was especially due to the content of polyunsaturated fatty acids and vitamin D in fish. Further, VKM concluded that the contaminants which could pose a potential risk to public health through fish consumption mainly were methylmercury, dioxins and dioxin-like PCBs. The Norwegian Food Safety Authority thus requests VKM to perform a reassessment with focus on the following:

- Nutrients
 - n-3 fatty acids: Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)
 - Vitamin D
 - Minerals iodine and selenium
- Contaminants
 - Dioxins and dioxin-like PCBs
 - Mercury

Terms of reference as provided by the Norwegian Food Safety Authority

The Norwegian Food Safety Authority (NFSA) requests an update of the benefit-risk assessment: "A comprehensive assessment of fish and other seafood in the Norwegian diet". NFSA asks VKM to base the updated assessment on the new knowledge about fish and fish consumption and to specifically address the following issues:

1. What are the main changes in the use of raw materials in feed, and how are these changes reflected in the levels of nutrients, dioxins and dioxin-like PCBs and mercury?
2. To what extent have levels of nutrients and contaminants in fish changed since 2006? Describe this change.
3. Calculate the intake of these substances on the basis of recent dietary data.
4. Consider the benefits of eating fish with regard to the intake of nutrients and the risks associated with the intake of dioxins, dioxin-like PCBs and mercury.
5. Does this change the conclusions from the report in 2006?
6. On the basis of updated knowledge, please comment if other substances, like pesticide and drug residues, which are not listed, could affect the conclusions with regard to the impact on public health?

The NFSA will use VKM's benefit-risk assessment both nationally and internationally. We therefore request that the assessment is written in English with a summary in Norwegian.

Assessment

1 Introduction and definition of terms

Fish is an integral component of a balanced diet (Norwegian Directorate of Health, 2014; Norwegian National Council for Nutrition, 2011) providing an important source of well-balanced protein, and important nutrients such as long-chain marine n-3 polyunsaturated fatty acids (n-3 LCPUFAs), vitamin D, iodine and selenium. There is evidence of beneficial effects of fish consumption on specific health outcomes, i.e. cardiovascular disease and optimal neurodevelopment, and it is assumed that marine n-3 fatty acids play an important role in the health-promoting effects of fish. However, it is also known that certain fish species constitute a source of exposure to chemical contaminants like dioxins, PCBs and mercury.

In Norway, fish consumption has traditionally been high, and lean fish has been dominating. However, in recent years, the consumption of farmed fish, particularly farmed Atlantic salmon, has increased considerably.

In recent years, concerns about the potential health risks associated with exposure to contaminants from food have resulted in strong focus on chemical management and policy both nationally and internationally. Stricter controls, use-restrictions and bans (the Stockholm Convention; see Glossary) of the most important persistent organic pollutants, have resulted in significant decline in concentrations of the most hazardous chemicals, i.e. PCBs, dioxins, persistent pesticides and brominated flame retardants, the last 20 years, both in the environment and in humans. Fish, as other food, contain both beneficial (i.e. nutrients) and potential hazardous compounds like dioxins, dl-PCBs and mercury, and the weighing of benefits and risks of food/fish consumption has become a main public health issue although the main focus has been on possible risks.

In 2006, the Norwegian Scientific Committee for Food Safety (VKM) conducted an assessment of the nutritional benefits of consuming fish and seafood, compared with the health risks associated with the intake of contaminants and other undesirable compounds that fish and other seafood may contain. In 2006, VKM concluded: "Consumption of fatty fish in particular provides important nutrients such as vitamin D and marine n-3 fatty acids. The consumption of fish in general and of marine n-3 fatty acids is important for preventing and impeding the development of cardiovascular disease. Marine n-3 fatty acids are important for pregnancy and foetal development as well" (VKM, 2006).

Since 2006 the data bases on both nutrient and contaminant concentrations in both wild and farmed fish have been improved substantially and updated information on fish consumption in 2-year olds, adults (18-70 years of age) and pregnant women is available from two more recent food consumption surveys, Småbarnskost 2007 (Kristiansen et al., 2009) and Norkost

3 (Totland et al., 2012) and from the Norwegian Mother and Child Cohort Study (MoBa) (Magnus et al., 2006), respectively. Also, large prospective cohort and population studies have been conducted since 2006, assessing fish consumption and associations with different health outcomes.

On this basis VKM has been asked by the Norwegian Food Safety Authority (NFSA) to conduct an updated comprehensive benefit-risk assessment of fish in the Norwegian diet (see Terms of reference from the NFSA). This assessment should also take into consideration that feed used in farming of Atlantic salmon and rainbow trout have changed the last 10 years, resulting in changes in both levels and composition of nutrients and contaminants in the farmed fish fillets. With regard to contaminants, the main focus was to be on dioxins, dioxin-like PCBs (dl-PCBs) and mercury. However, VKM was also asked to comment if other substances, like plant and medicine residues could affect the conclusions with regard to impact of fish consumption on public health.

In this report, the associations between fish consumption and neurodevelopment and other health outcomes related to the central nervous system, cardiovascular disease, cancer, type-2 diabetes and metabolic outcomes, and asthma/allergy/atopy, are examined, as well as the risks from exposure to the contaminants dioxins, dl-PCBs and methylmercury contributed by fish. VKM has also made various scenarios to foresee how possible changes in fish consumption pattern and amounts will affect the contribution from fish to recommended intakes of specific essential nutrients and tolerable intakes of specific contaminants. The contribution to total dioxins and dl-PCBs from sources other than fish is considered only in scenarios where a simple model estimate of weekly intake of dioxins and dl-PCBs in adults from various amounts of farmed salmon and other food is done.

VKM has not systematically weighted the evidence from national and international comprehensive reports, or graded the results reported in reviews/meta-analyses and individual studies, but summarised the results. Single studies from the Nordic region were included because they were considered of special relevance. In addition, single studies published in 2014 were included in order to cover the most recent information.

The purpose of this report is to update the comprehensive assessment of fish and other seafood in the Norwegian diet from 2006, by addressing the benefits and risks from fish consumption, and thus provide a foundation for Norwegian food authorities in preparing advice on fish consumption for the Norwegian population.

Definition of terms: The term “fish” used in this report is defined as finfish (vertebrates), whether of marine or freshwater origin, farmed or wild. Marine mammals, shellfish (invertebrates), as well as sustainability issues and environmental impacts, although important, are considered to be outside the scope of this report since it was not requested in the Terms of reference. This is in contrast to the VKM assessment from 2006, which included both fish and other seafood.

Persistent lipophilic contaminants like PCBs and dioxins will accumulate in fatty tissue and biomagnify in the marine food chains. Organic metals, like mercury, will also accumulate in the marine food chain, and the concentrations increase with age and size of the individual. Thus, it is expected to find the highest concentrations of PCBs and dioxins in fatty tissue, such as fillets of mackerel, herring and salmon, and in the liver of e.g. cod, while the highest mercury concentrations are found in old individuals of lean fish constituting top of marine food chain, such as pike and tuna. Fish is the only dietary source of methylmercury, which constitutes about 80-100% of total mercury in fish. For dioxins and PCBs there are several important dietary sources in addition to fish and other seafood. VKM uses the reference values set by international risk assessment bodies as basis for risk characterization of contaminant exposure from fish in the present opinion.

N-3 polyunsaturated fatty acids (n-3 PUFAs) contain one of the double bonds located at three carbon atoms from the methyl end. The main n-3 PUFAs in the diet are alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA). EPA, DPA and DHA are usually referred to as n-3 LCPUFAs, i.e. n-3 PUFA with 20 or more carbon atoms (EFSA, 2010b; EFSA, 2012b). Thus, in this assessment the term n-3 LCPUFA refers to EPA, DPA and DHA and does not include ALA, which has carbon chain of 18 atoms. VKM uses mainly the national reference values of nutrients intake for benefit characterisation of the specific nutrients intakes from fish. For n-3 LCPUFAs, comparison is also done with European recommendations.

Existing dietary guidelines for fish consumption: It has long been recognized by health authorities, both nationally and internationally, that fish consumption and n-3 LCPUFA from fish are beneficial to human health. In the report on "Diet, nutrition and chronic diseases" from WHO (2003), a regular fish consumption (1-2 servings per week) is recommended to protect against coronary heart disease and ischaemic stroke (WHO, 2003). Each serving should provide an equivalent of 200-500 mg EPA and DHA. In June 2014, the US Food and Drug Administration (FDA) and the US Environmental Protection Agency issued an updated draft advice for fish consumption encouraging pregnant women and breastfeeding mothers to eat more fish low in mercury (EPA/FDA, 2014). The updated advice is in line with the 2010 Dietary guidelines for Americans.

In 2006, the Norwegian recommendation for fish consumption merely was to eat more fish both for dinner and as bread spreads. As a consequence of results presented in the VKM opinion on fish from 2006 and the report from the Norwegian National Council for Nutrition, "Dietary advice to promote public health and prevent chronic diseases in Norway" (Norwegian National Council for Nutrition, 2011), these recommendations were altered and made quantitative by the Norwegian Directorate for Health, which currently recommends fish as dinner meal 2-3 times per week for all age groups (Norwegian Directorate of Health, 2014). Fish is also recommended as bread spread. This recommendation represents totally 300-450 g fish per week for adults, and less for children. For adults, at least 200 g should be fatty fish, such as salmon, trout, mackerel or herring. Six portions of bread spreads represents approximately one dinner portion. A clarification is given for young females and

pregnant women. They should, over time, avoid eating more than two meals of fatty fish per week, including fish like salmon, trout, mackerel and herring. In addition to the general recommendation to eat 300-450 g fish per week, the NFSA continuously issues regional advice to restrict consumption of fish caught in certain polluted fjords and harbours and fish species known to have high concentrations of pollutants (www.matportalen.no).

2 Update of reference values for selected nutrients and undesirable substances

The majority of health authorities worldwide recommend a regular fish intake in order to ensure proper nutrition and health benefits. There are also updated recommendations for intake of several key nutrients present in fish, such as the n-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), vitamin D and selenium. After 2006, new reports and risk assessments concerning the contaminants (dioxins, mercury) present in fish have emerged.

2.1 Recommendations for selected nutrients contributed from fish

The FAO/WHO report on the risks and benefits of fish consumption (FAO/WHO, 2011) concluded that: "The health attributes of fish are most likely due in large part to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Fish, however, contain other nutrients (e.g. protein, selenium, iodine, vitamin D, choline and taurine) that may also contribute to the health benefits of fish consumption.

The sections below are based on the Norwegian dietary recommendations (Norwegian Directorate of Health, 2014), which are based on the 5th updated version of the Nordic Nutrition Recommendations (NNR5, 2012). Other sources include the scientific reports "Dietary advice to promote public health and prevent chronic diseases in Norway" (Norwegian National Council for Nutrition, 2011), "Evaluation of negative and positive health effects of n-3 fatty acids as constituents of food supplement and fortified foods" (VKM, 2011b) and "Scientific Opinion on Dietary Reference Values for fats, including saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, trans fatty acids, and cholesterol" (EFSA, 2010b).

The Norwegian recommendations for n-6 and n-3 polyunsaturated fatty acids are given as energy percent for the two essential fatty acids linoleic acid (LA, 18:2n-6) and alpha-linolenic acid (ALA, 18:3n-3) and no recommendation is given for the n-6 to n-3 ratio (Norwegian Directorate of Health, 2014). The main focus of this evaluation regarding fatty acids is the amount of EPA, DPA and DHA provided from fish and fish oil supplements.

2.1.1 N-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)

Eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA) and docosahexaenoic (DHA) are important structural components of cell membranes and contribute to various membrane

functions such as fluidity, permeability, activity of membrane-bound enzymes and receptors, and signal transduction (FAO/WHO, 2011; VKM, 2011b).

Norway does not give any specific recommendations for dietary intake of EPA, DPA or DHA but based on the 5th edition of the Nordic Nutrition Recommendations (NNR5, 2012) the Norwegian Directorate of Health now recommends a daily intake of 200 mg DHA for pregnant and lactating women (Norwegian Directorate of Health, 2014).

In 2010, EFSA published a scientific opinion on population reference intakes for the European population on fat, including EPA and DHA (EFSA, 2010b). It concluded that with respect to cardiovascular diseases, prospective epidemiological and dietary intervention studies indicate that oily fish consumption or dietary n-3 long-chain polyunsaturated fatty acids supplements (equivalent to a range of 250 to 500 mg of EPA+DHA daily) decrease the risk of mortality from coronary heart disease (CHD) and sudden cardiac death. An intake of 250 mg/day of EPA+DHA appears to be sufficient for primary prevention in healthy subjects. Therefore, and taking into account that available data are insufficient to derive an average requirement, the Panel proposed to set an Adequate Intake of 250 mg for EPA+DHA for adults based on cardiovascular considerations. To this intake 100 to 200 mg of preformed DHA (i.e. DHA from fish or supplements) should be added during pregnancy and lactation to compensate for oxidative losses of maternal dietary DHA and accumulation of DHA in body fat of the foetus or infant. In older infants, DHA intakes at levels of 50 to 100 mg/day have been found effective for visual function in the complementary feeding period and are considered to be adequate for that period. The EFSA Panel proposed an Adequate Intake of 100 mg DHA for older infants (older than 6 months of age) and young children below the age of 24 months. EFSA states that the currently available evidence does not permit to define an age specific quantitative estimate of an adequate dietary intake for EPA and DHA for children aged 2 to 18 years. However, dietary advice for children should be consistent with advice for the adult population (i.e., 1 to 2 fatty fish meals per week, and for adults equivalent to ~250 mg of EPA+DHA per day) (EFSA, 2010b). KM previously concluded that based on the reviewed literature, it was not possible to identify clear adverse effects from EPA and DHA, which would be a prerequisite for setting tolerable upper intake levels (VKM, 2011b).

2.1.2 Vitamin D

The role of vitamin D in the development and maintenance of bone is well established, and vitamin D has been associated with numerous health outcomes. Vitamin D regulates serum calcium and phosphate levels, and may modify immune function, cell proliferation, differentiation and apoptosis (Basit, 2013). Current evidence from systematic literature reviews indicates that vitamin D intake and status is associated with fractures and falls, cardiovascular outcomes, and total mortality (Bjelakovic et al., 2014; Lamberg-Allardt et al., 2013; Zheng et al., 2013b).

Vitamin D is primarily synthesised in the skin on exposure to sunlight, when skin is subjected to UV radiation. During winter months in northern European countries, UV radiation is not strong enough for vitamin D production and the body has to rely on body stores and dietary sources. Vitamin D occurs naturally in foods as vitamin D₂ (ergocalciferol) and vitamin D₃ (cholecalciferol). In the 5th edition of the Nordic Nutrition Recommendations (NNR5, 2012), and consequently the Norwegian dietary guidelines from 2014, the recommended intake for vitamin D was increased from 7.5 µg to 10 µg/day for children above two years and adults, and to 20 µg/day for the elderly (75 years or older) (Table 2.1.2-1) (NNR5, 2012; Norwegian Directorate of Health, 2014). The reason behind the increased recommendation is new scientific data that has emerged after 2004. As in the 4th edition of the Nordic Nutrition Recommendations (NNR4, 2004), serum 25-hydroxy-vitamin-D (25OHD) concentrations of more than 50 nmol/L was upheld as an indicator of sufficient vitamin D status.

For people with little or no sun exposure, the recommended intake is now 20 µg/day. This can be achieved by taking a daily supplement of 10 µg vitamin D₃ in addition to the dietary intake, or by choosing foods rich in vitamin D. For the elderly (75 or older), the recommended intake can be achieved by selecting foods naturally high in vitamin D and vitamin D-enriched foods in combination with a supplement if necessary (NNR5, 2012).

Taking into consideration that both EFSA and the US Institute of Medicine (IOM) have increased the tolerable upper intake level (UL) for vitamin D (EFSA, 2012c; IOM, 2010) this was also applied to the NNR5 (2012). The UL for adults and adolescents (11-17 years) was increased from 50 to 100 µg/day. For younger children, UL was set to 50 µg/day and for infants (0-12 months) the UL was set at 25 µg/day. The average requirement (AR) and lower intake level (LI) for vitamin D were set to 2.5 and 7.5 µg/day, respectively (Table 2.1.2-1).

Table 2.1.2-1 Vitamin D recommendations in Nordic Nutrition Recommendations, 5th edition (NNR5, 2012)

Vitamin D	Females (2-74 years) µg/day	Males (2-74 years) µg/day	Children (0-24 months)^a µg/day	Elderly (≥75 years) µg/day
Recommended intake	10 ^b	10	10	20
Average requirement	7.5	7.5	-	-
Lower intake level	2.5	2.5	-	-
Upper intake level	100 ^c	100 ^c	-	-

^aFrom 1-2 weeks of age, infants should receive 10 µg vitamin D₃ per day as a supplement.

^b10 µg/day also for pregnant and lactating women.

^cEFSA (2012c); IOM (2010)

- not given any average requirement, lower or upper intake levels.

2.1.3 Iodine

Iodine is important for normal functioning of the thyroid gland and production of the hormones thyroxine (T₄) and triiodinethyroxine (T₃). A deficiency of iodine in the diet is

associated with enlargement of the thyroid gland (thyroidea), the development of goiter resulting in effects such as arrested growth and mental retardation in children, and low metabolism, reduced blood pressure and weakness of the muscles in adults. Iodine deficiency is considered by WHO to be “the single most important preventable cause of brain damage” worldwide (WHO et al., 2007) Insufficient iodine status is not only a problem in developing countries, but is a major public health problem in many countries in Europe and in Australia, New Zealand and the US (Brantsaeter et al., 2013; Pearce et al., 2013; Vanderpump et al., 2011).

In the Nordic Nutrition Recommendations 5th edition (NNR5), and consequently the Norwegian dietary guidelines, no change to the previous recommended intake of iodine was applied. The experts evaluating new scientific evidence concluded that there were not new data supporting changes (NNR5, 2012). In the 4th edition of the Nordic Nutrition Recommendations (NNR4, 2004) the estimated average requirement (AR) was set at 100 µg/day for both adult men and adult women. The recommended intake was set at 150 µg/day to include a safety margin for any goitrogenic substances in foods. The lower intake level in adults was set at 70 µg/day for both sexes (Table 2.1.3-1). The UL is 600 µg/day.

Table 2.1.3-1 Iodine recommendations in the Nordic Nutrition Recommendations, 5th edition (NNR5, 2012)

Iodine	Women µg/day	Men µg/day	Children (2-5 years) µg/day	Children (6-9 years) µg/day	Children (10-13 years) µg/day
Recommended intake	150 ^a	150	90	120	150
Average requirement	100	100	-	-	-
Lower intake level	70	70	-	-	-
Upper intake level	600	600	-	-	-

^aFor pregnant women: 175 µg, and lactating women: 200 µg/day.
- not given any average requirement, lower or upper intake levels.

EFSA published a Scientific Opinion on dietary reference values for iodine in May 2014. A recommendation for adequate intake (AI) of 150 µg/day is proposed for adults. For infants aged seven to 11 months and for children, AIs range between 70 µg/day and 130 µg/day. For pregnant women and lactating women, an AI of 200 µg/day is proposed, taking into account the additional needs (EFSA, 2014a).

UNICEF/ ICCIDD/WHO in 2007 increased the recommendation for iodine from 200 to 250 µg/day for pregnant, which is also their recommendation for lactating women (WHO et al., 2007). The reason behind this is pregnant women and infants are exceptionally vulnerable to deficiency. In the NNR5 and Norwegian dietary recommendations, the recommended iodine intake for pregnant and lactating women was kept at 175 and 200 µg/day, respectively.

2.1.4 Selenium

Selenium is an essential trace element that plays an important role as cofactor for enzymes involved in protection against oxidative damage and regulation of immune function. Selenium is also important in the detoxication of various heavy metals (Alexander, 2015). Low selenium status has been associated with increased risk of mortality, poor immune function, and cognitive decline, but supplementation is problematic due to the narrow range of recommended intake, and selenium supplementation may adversely affect people with adequate status (Rayman, 2012).

The recommended intake of selenium was updated in Nordic Nutrition Recommendations 5th edition (NNR5) and the Norwegian dietary guidelines (Norwegian Directorate of Health, 2014), resulting in an increase from 50 µg/day for men and 40 µg/day for women to 60 µg/day for men and 50 µg/day for women (Antypa et al., 2012). The recommended intake during pregnancy and lactation is increased from 55 to 60 µg/day and the recommended intake for children is increased to 25, 30 and 40 µg/day for different age groups based on extrapolation from the adult values (Table 2.1.4-1). For adults, the UL is unchanged at 300 µg of selenium per day.

Table 2.1.4-1 Selenium recommendations in the Nordic Nutrition Recommendations, 5th edition (NNR5, 2012)

Selenium	Women µg/day	Men µg/day	Children (2-5 years) µg/day	Children (6-9 years) µg/day	Children (10-13 years) µg/day
Recommended intake	50 ^a	60	25	30	40
Average requirement	30	35	-	-	-
Lower intake level	20	20	-	-	-
Upper intake level	300	300	-	-	-

^aFor pregnant and lactating women: 60 µg/day.

- not given any average requirement, lower or upper intake levels.

2.2 Contaminants and some other undesired substances in fish—possible hazards and established tolerable intakes

Fish can contribute significantly to the dietary exposure to some contaminants, of which the most important are methylmercury and the dioxins and dioxin-like PCBs (dl-PCBs). For these substances, parts of the population have previously been reported to exceed the tolerable intakes.

A tolerable intake is the amount of a substance, or substance group, which can be consumed safely throughout a person's lifetime without appreciable risk of adverse health effects. Tolerable intakes are set by large international risk assessment bodies, such as WHO or EFSA, and incorporate safety margins, in order to protect all parts of the population, including the most vulnerable parts of the population. Tolerable intakes can be set on a

daily, weekly or monthly basis, depending on the characteristics of the substance in question. Exceedance of tolerable intakes is undesirable and may represent a risk to human health if repeated frequently. The purpose of this chapter is to summarise and update recent reports/risk assessments of contaminants that are most relevant for fish. VKM uses the reference values set by international risk assessment bodies (Table 2.2-1) as basis for risk characterization of contaminant exposure from fish in the present opinion.

Table 2.2-1 Tolerable intakes for some persistent organic pollutants present in fish

Contaminant	Tolerable intake	Reference
Methylmercury	1.3 µg/kg bw/week	EFSA (2012a)
Inorganic mercury	4.0 µg/kg bw/week	EFSA (2012a);JECFA (2010)
Dioxins and dl-PCBs	14 pg TE/kg bw/week	SCF (2001)
Dioxins and dl-PCBs	70 pg TE/kg bw/month	JECFA (2001)
PCB-6^a	10 ng PCB-6/kg bw/day ^b	VKM (2008)
PFOS	150 ng/kg bw/day	EFSA (2008)
PFOA	1.5 µg/kg bw/day	EFSA (2008)

^aSum of PCB-28, -52, -101, -138, -153, -180

^breference value used by VKM in 2008, not a tolerable intake

2.2.1 Mercury

Mercury is released into the environment from both natural and anthropogenic sources. Once released, mercury undergoes a series of complex transformations and cycles between atmosphere, ocean and land. The three chemical forms of mercury are (i) elemental or metallic mercury (Hg⁰), (ii) inorganic mercury (mercurous (Hg₂²⁺) and mercuric (Hg²⁺) cations) and (iii) organic mercury. Methylmercury is by far the most common form of organic mercury in the food chain, and after oral intake, methylmercury is much more extensively and rapidly absorbed than mercuric and mercurous mercury. Seafood is the main dietary source of both inorganic mercury and methylmercury exposure (EFSA, 2012a), and the only important dietary source of methylmercury.

2.2.1.1 Methylmercury

Methylmercury accumulates in the body and crosses the placenta- and blood-brain barriers. Total mercury in hair and blood are routinely used as biomarkers of methylmercury exposure. Hair contains almost exclusively methylmercury, whereas blood contains both inorganic and methylmercury. However, in fish-eating populations the blood methylmercury concentration is much larger than the inorganic mercury concentration and therefore serves as a good biomarker of methylmercury exposure.

Unborn children constitute the most vulnerable group for developmental effects of methylmercury exposure. EFSA in 2012 reduced the tolerable weekly intake (TWI) for methylmercury from 1.6 (set by WHO in 2004) to 1.3 µg/kg bw/week, expressed as mercury, based on recent findings of neurodevelopmental effects in prenatally exposed children at

slightly lower methylmercury exposure than previously reported (EFSA, 2012a). EFSA calculated that mean exposure in Europe (all population groups) is below the TWI, whereas 95th percentile exposure is in the range of or exceeding the TWI. This was confirmed by reported levels in hair and blood in Europe.

In general, all mercury in other food groups than fish and other seafood is believed to be inorganic, and there are no other substantial dietary sources.

2.2.1.2 Inorganic mercury

The kidney is sensitive to inorganic mercury toxicity. Inorganic mercury is also toxic to the liver, the nervous system and the immune system, and is also a reproductive and developmental toxicant.

EFSA recently established a tolerable intake of inorganic mercury of 4.0 µg/kg bw/week, expressed as mercury, based on kidney toxicity (EFSA, 2012a). This was in line with the evaluation from the JECFA in 2010 (JECFA, 2010).

2.2.1.3 Time-trends of mercury exposure in Norway

Time-trends on human exposure levels in Norway were not available. There are indications of increasing levels of mercury in freshwater fish in Norway (Braaten et al., 2014; NIVA, 2009) and Sweden (Akerblom et al., 2012). A report from the OSPAR commission in 2009 on trends and concentrations of selected hazardous substances in sediments and biota (OSPAR Commission, 2009) stated that background concentrations of mercury are found in fish and shellfish at some stations in Ireland, Scotland, and western Norway. They reported that both upward and downward temporal trends in fish and shellfish occur in the North East Atlantic, with a grouping of generally upward trends in southern Norway (stations along the south-east and-south west coast).

2.2.2 Dioxins and polychlorinated biphenyls (PCBs)

Dioxins and PCBs are closely related groups of chlorinated organic compounds and constitute a subgroup among the persistent organic pollutants (POPs). They are fat-soluble and persistent to degradation, they bioaccumulate and are biomagnified in the environment. They are found in the highest concentrations in organisms located high up in the food chain. Fat of animal origin, and in particular marine fat, is the major dietary exposure source.

The term 'dioxins' usually encompasses both the 75 chlorinated dibenzo-p-dioxins (PCDDs) and 135 chlorinated dibenzofurans (PCDFs). There are 209 different PCB congeners. The chemical properties and toxicological effects of dioxins and PCBs vary according to the number and positions of the chlorine atoms on the aromatic rings.

Of the 209 possible PCB congeners, 12 are included in the group of dioxin-like PCBs (dl-PCBs) and are evaluated together with the dioxins, since they share mechanism of action

with the most toxic dioxins. The rest of the PCBs are referred to as non-dioxin-like PCBs (ndl-PCBs).

2.2.2.1 Dioxins and dioxin-like-PCBs

The toxicity of 17 dioxins and 12 dioxin-like PCBs (dl-PCBs) is related to binding and activation of the transcription factor Ah (aryl hydrocarbon) receptor, also known as the TCDD or dioxin receptor. These substances have been assigned toxic equivalency factors (TEF) in relation to 2,3,7,8-TCDD, which is the most potent dioxin congener and has a TEF of 1. The total amount of toxic equivalents (total TEQ) in a sample is calculated by multiplying the concentration of each congener with the associated TEF and then adding up the contributions from the different congeners. The total TEQ in a sample is an estimate of the total dioxin effect, which is a simplified method for making risk assessments of dioxin/PCB-mixtures. The WHO-TEFs were set in 1998 (WHO₁₉₉₈-TEF) and revised in 2005 (WHO₂₀₀₅-TEF).

Abnormal activation of the Ah-receptor may disrupt cell function by altering the transcription of vast array of genes whose activities are involved in a number of processes, including growth regulation and development. The most significant hazardous effects on health resulting from chronic exposure to dioxins and dl-PCBs are impairment of the reproductive system, a weakened immune system, impairment of the endocrine system and neurotoxic and carcinogenic effects. Dioxins have been classified as carcinogenic to humans (Group 1) by IARC (IARC, 1997), but they are not genotoxic (JECFA, 2001; SCF, 2001). The critical effect used in risk assessment was reproductive effects in rats that were exposed prenatally. Risk assessments performed by SCF and JECFA took into account the large difference in biological half-life of TCDD between rats and humans (i.e. about one month versus 7.5 years), the insufficiency of the toxicological database, and limited knowledge about the variation in the biological half-lives in different population groups. The TWI established by SCF is 14 pg TEQ/kg bw/week (SCF, 2001). JECFA's assessment is comparable with that of SCF, except that JECFA expresses the tolerable intake level on a monthly basis (70 pg TEQ/kg bw/month) (JECFA, 2001).

2.2.2.2 Non-dioxin-like PCBs

The presence of non-dioxin-like PCBs (ndl-PCBs) has been expressed as the sum of three PCB congeners (PCB-138, -153 and -180) or PCB-6 (PCB-28, -52, -101, -138, -153, -180), or as PCB-7, which in addition to PCB-6 includes PCB-118 (a dl-PCB). Sometimes the PCB concentration has been expressed as total PCBs. PCB-153 is often used as an indicator of total PCB or PCB-6, because the correlation between PCB-153 and PCB-6 is high.

IARC has in 2013 classified PCBs in Group 1, i.e. carcinogenic to humans. According to IARC, the carcinogenicity of PCBs cannot be solely attributed to the carcinogenicity of the dioxin-like PCBs (Lauby-Secretan et al., 2013). In epidemiological studies, the most important adverse health effects associated with exposure from food and the environment were related

to perinatal PCB exposure and the impairment of reproduction, including delayed development of the central nervous system and an impaired function of the immune system. According to EFSA (2005), it was not possible to distinguish between the effects resulting from dioxins and dl-PCBs and the effects resulting from ndl-PCBs. This is because exposure to ndl-PCBs is normally highly correlated with exposure to dioxins and dl-PCBs. Furthermore, in many experimental studies the PCB test substance has been contaminated with dioxins. As a result, EFSA concluded that it is not possible to establish a tolerable intake level for ndl-PCBs (EFSA, 2005).

Neurotoxic effects of ndl-PCBs are well known. The ndl-PCBs act via several different mechanisms and not via the AhR. Mechanistic studies indicate that they may affect components of the nervous system in several different ways. They alter intracellular signal transduction pathways by interfering with intracellular sequestration of calcium and increase activation of protein kinase C (PKC). Induction of apoptosis and increased production of reactive oxygen species and changes in levels of neurotransmitters such as dopamine and acetylcholine have been reported. The latter is suggested to be linked to interference with PCB on thyroid hormone levels because cholinergic fibres are particularly sensitive to thyroid hormone deficiency. Furthermore, increased release of arachidonic acid has been observed. Changes in the PKC signalling pathway and calcium homeostasis as well as reduced dopamine levels has been confirmed in animal studies (EFSA, 2005).

A provisional tolerable intake of 20 ng/kg bw/day for all 209 PCB congeners was proposed at the 2nd PCB workshop in Brno (Czech Republic, May 2002) and has been used in France, the Netherlands, and Norway (AFSSA, 2007; Baars et al., 2001; VKM, 2008). This corresponds to a provisional tolerable daily intake of 10 ng PCB-6/kg bw/day, since half the total intake of PCBs consists of PCB-6.

In 2003, AFSSA adopted a reference dose of 20 ng/kg bw/day for all 209-PCB congeners, and a tolerable daily intake of 10 ng PCB-6/kg bw/day, since half the total intake of PCBs consists of PCB-6 (AFSSA, 2007). The reference dose was derived from the BMDL (see Glossary) from human studies described in the EFSA opinion from 2005. In 2008, VKM used 10 ng PCB-6/kg bw/day as a reference value in an evaluation of whether the TWI for dioxins and dl-PCBs was also protective to ndl-PCBs exposure from the diet, given the relative composition of dioxins, dl-PCBs and ndl-PCBs in the food consumed by in Norway. VKM concluded that with the combination of dioxins and PCBs in Norwegian food, exposure to dioxins below the TWI would also protect against toxicological effects from exposure to ndl-PCBs (VKM, 2008).

2.2.2.3 Time-trends of dioxin and PCB exposure in Norway

Dioxins and PCBs are commonly determined in blood or breast milk, and concentrations are generally expressed per unit of fat in the sample, reflecting that these substances are highly fat soluble. Since dioxin/PCB concentrations in the body lipids are quite similar, other tissue

(e.g. fat tissue or cord blood) can also provide information on contaminant exposure levels in humans.

From 1986 to 2005 the concentration of dioxins and dl-PCBs and ndl-PCBs in breastmilk from first time mothers in Norway decreased by approximately 70% (VKM, 2013a). This reflects falling environmental levels and therefore falling levels in food, leading to lower dietary exposure. A similar decrease has also been reported up to 2007 in men from Northern Norway (Nost et al., 2013). More recent time-trend data were not available.

2.2.3 Other contaminants

A large number of substances in the group of chlorine-, fluorine or bromine-substituted organic compounds can represent a hazard to human health and be present in fish. This applies to dioxins, PCBs, campheclor (toxaphene), dichlordiphenyltrichlorethane (DDT) and its metabolites (DDD and DDE), chlordane, dieldrine, aldrin, endrin, heptachlor, hexachlorbenzene (HCB), chlorinated cyclohexane, brominated flame retardants such as polybrominated diphenylethers (PBDEs) and fluorinated compound such as PFOS and PFOA.

Such substances are found in the highest concentrations in organisms located high up in the food chain. Fat of animal origin, and in particular fat of marine origin, can be the major exposure source. Most of these compounds are however no longer in use, and since also cleaning of industrial emissions has been implemented, the levels in the environment are generally declining.

With fluorinated compounds the situation is different, see below.

Also organotin substances, which have been used as anti-fouling agents on ships for decades until their use was banned, can be present in fish from fjords and harbour areas. However, since the main bulk of fish on the market are not caught close to harbours, organotin substances are not addressed further in this opinion.

2.2.3.1 Polybrominated flame retardants

Polybrominated diphenyl ethers (PBDEs) are to some extent structurally related to ndl-PCBs. Three commercial mixtures of PBDEs (penta-, octa- and deca-BDEs) have been used as flame retardants, and their composition is reflected in food and environment. These substances have in addition potential for long-range atmospheric transport.

Penta- and octa-BDE, as substances, in mixtures and in products are banned both in EU and Norway, and also globally via the POP regulation (the Stockholm Convention).

Since 2008, it has been prohibited to manufacture, import, export, place on the market and use substances and mixtures containing 0.1% or more of decaBDE in Norway. The regulation also applies to products and parts of products containing 0.1% or more of decaBDE. Some derogations are given.

The European Chemicals Agency (ECHA), in collaboration with the Norwegian Environment Agency, has recently proposed a European restriction within the REACH regulation on the manufacturing, use and placing on the market of decaBDE. The restriction proposal is on public consultation until March 2015 and will also be reviewed by the ECHA Committees for Risk Assessment (RAC) and Socio-economic Analysis (SEAC) before any new regulation could be adopted. In parallel with this process, the Norwegian Environment Agency has proposed a globally ban on decaBDE via the POP regulation.

Food is a main PBDE exposure source in humans, however, there are large individual differences and dust can be a major source, especially in children. The congeners most commonly occurring are BDE-47, BDE-99, BDE-100, BDE-153 and the fully brominated BDE-209. In Norway, highest mean dietary exposure was seen for BDE-47 (mean 0.97 ng/kg bw/day) and BDE-209 (1.5 ng/kg bw/day), and the major dietary sources were fish (BDE-47) and dairy products (BDE-209) (Thomsen et al., 2008). In different European countries, EFSA estimated in 2011 that the exposure to BDE-47 ranged between 0.29 and 1.91 ng/kg bw/day, whereas that of BDE-209 ranged between 0.35 and 2.85 ng/kg bw/day (EFSA, 2011).

The concentrations of PBDEs in blood from Norwegians are in the same range as those in the rest of Europe, but approximately 10-fold lower than in blood from inhabitants in the USA. After a strong increase in concentration of PBDEs in blood during the 90-ties, the levels of some PBDEs have been falling the latter years, whereas for other the increase has leveled off.

Effects reported in experimental rats and mice after exposure to different PBDEs include induction of liver enzymes, effects on thyroid hormone levels, reproductive effects and disturbed neurodevelopment.

No tolerable intakes for PBDEs have been set by EFSA due to lack of sufficient knowledge about their toxicities. However, the margin between concentrations that cause low toxic effects in experimental animals and those seen in European populations appear to be large, and EFSA concluded that the risk of adverse health effects is low (EFSA, 2011).

EFSA (2011) also concluded that it was inappropriate to use BMDL to establish a health based guidance value, and instead used a margin of exposure (MOE) approach for the health risk assessment of hexabromcyclododecanes (HBCDs or HBCDDs). Since elimination characteristics of HBCDs in animals and humans differ, the Panel used the body burden as starting point for the MOE approach. EFSA (2011) concluded that current dietary exposure to HBCDs in the European Union does not raise a health concern.

2.2.3.2 Fluorinated substances

Fluorinated substances have been widely used for decades because of their water and oil repellent abilities, but they did not gain much attention until approximately ten years ago. Although substances in this class are associated with plasma proteins and are not fat-

soluble, they are persistent and the highest concentrations are found in organisms high up in the food chain. Perfluorooctanosulphonate (PFOS) and perfluorooctanoic acid (PFOA) are found at highest levels in food, and food (particularly seafood) is the most important source of these contaminants. They are found in muscle from all kinds of fish (lean or fatty), but at higher levels in liver (Haug et al., 2010). Estimated intakes in Europe and Norway are low (PFOS: 0.27 to 5.2 ng/kg bw/day; PFOA 0.08-4.3 ng/kg bw/day). The TDIs set by EFSA in 2008 (for PFOS 150 ng/kg bw/day and for PFOA 1.5 µg/kg bw/day) are orders of magnitude higher than the dietary exposure.

2.2.4 Veterinary medicine residues in farmed fish

Sometimes it is necessary to treat farmed fish with veterinary medicinal products (VMPs). When farmed fish is medicated, several measures are taken to ensure food safety for the consumer.

- Only authorized veterinarians/aquamedicine biologists can prescribe approved veterinary medicinal products.
- Only therapeutic agents that have been evaluated and approved in accordance with the EU regulations can be applied. For each substance and animal group, Maximum Residue Limits (MRLs) have been established.
- Withdrawal times for medicated fish are applied.

Withdrawal time denotes the time from completion of therapy with a veterinary medicinal product (VMP) until slaughtering of the fish can be done, and the purpose is to ensure that residual levels of the VMP in the fish are below the legal limit. The Norwegian Medicinal Agency is responsible for setting withdrawal times for VMPs holding a Norwegian marketing Authorisation. When setting maximum residue levels (MRLs) eventual effects of VMPs on future processing of food, and if the VMP has additional use (e.g. as pesticide) which could lead to additional exposure for the consumer, is taken into account as outlined in the The Norwegian Pharmaceutical Product Compendium (<http://www.felleskatalogen.no/medisin-vet/tilbakeholdelsestider>). The veterinarian or aquamedicine biologist initiating the therapy as well as the fish farmer is responsible to ensure that fish is not slaughtered during this period. All use of VMPs must be reported to the Norwegian Food Safety Authority (NFSA) by the veterinarian/aquamedicine biologist in charge of the use. It is mandatory for the fish farmer to submit plans for slaughtering before effectuation. These actions enable the NFSA inspector to control that withdrawal times have been complied with at fish slaughtering. The fish can be banned from slaughter if the withdrawal times are not being withheld.

To avoid the presence of residues of VMPs at levels that might cause harm for the consumers, acceptable legal residue concentrations in food producing animals have been established. According to current EU legislation (EU 37/2010) each substance is assigned a maximum residue level (MRL), which is the highest permitted residual concentration of legally applied pharmacologically active substances in products (food) intended for human consumption. Consumption of food with medicine residues below the MRL should, by a wide safety margin, not pose any health risk to the consumer. The MRLs for fish are set for

muscle and skin in natural proportions. For more details see the latest report on Monitoring program for pharmaceuticals, illegal substances, and contaminants in farmed fish (Hannisdal et al. 2014).

On behalf of the NFSA, the National Institute of Nutrition and Seafood Research (NIFES) carry out a continuous surveillance programme on veterinary medicinal products in seafood in accordance with EU Directive 96/23/EC. One sample per 100 tons of produced fish has been analysed each year since 1998. Samples have been collected by official inspectors from the NFSA at the farm, without prior notification to the farmer, and sampling has been done after the expiration of the withdrawal period. Additionally, samples representative of the farmed fish ready for the market have been collected at the slaughterhouse/processing plants.

According to Hannisdal et al. (2014), banned substances include growth promoters such as steroids and stilbenes, and substances listed in Commission Regulation (EU) No 37/2010 under prohibited substances for which MRLs cannot be established. Prohibited compounds considered relevant for aquaculture are chloramphenicol, nitrofurans, and metronidazole. To ensure harmonized levels for the control of banned substances, analytical methods used for banned compounds should meet minimum required performance limits (MRPLs) set by the community reference laboratories (CRLs), national reference laboratories (NRLs) and member states of the European Union (Commission Decision 2003/181/EC; Commission Decision 2004/25/EC; CRL Guidance Paper 2007).

During the years 1998-2013, more than 30 000 samples from farmed salmon have been analysed. So far (November 2014), no residues of banned substances or medicine residues above EU MRLs for VMPs including antibiotics have been detected in any of the samples.

Antibiotics

The use of antibiotics in farmed fish in Norway has been low since mid and late 1990 (NORM/NORM-VET, 2013). In relation to the biomass of farmed fish, there have been marginal changes in antibiotics sales during the latest years. The amount of antibiotics sold in recent years represents approximately one treatment in 0.5-1% of the fish.

Effective vaccines against bacterial infections in fish farming were developed in 1990s and the implementation of vaccination programmes of fish was established. This resulted in a major decrease in the usage of antibiotics in fish farming despite a rapid growth in the biomass slaughtered fish (Figure 2.2.4-1).

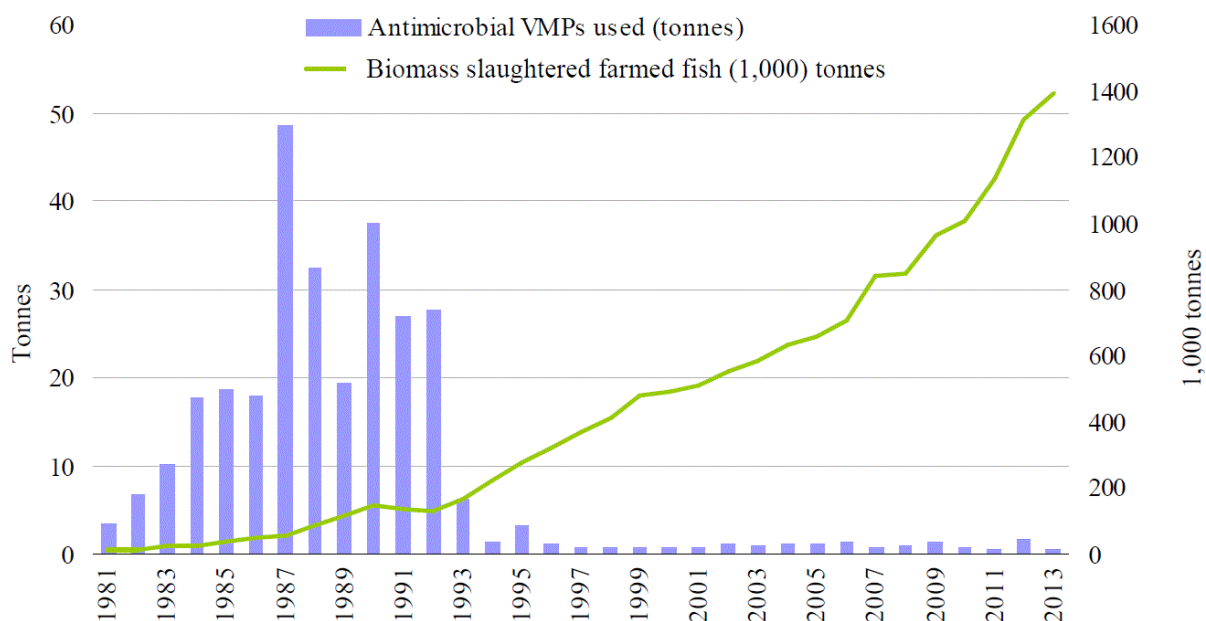


Figure 2.2.4-1 The total sale in tonnes of active ingredients of antibiotics sold in Norway and used in Norwegian farmed fish during the years 1981 to 2012, and the concurrent biomass farmed fish slaughtered during the same time span. Source: NORM/NORM-VET 2013 (with permission) (NORM/NORM-VET, 2013)

Agents against sea lice

Infestation caused by sea lice, an ectoparasite of salmonids in salt water, mainly *Lepeophtheirus salmonis*, is at present a challenging health issue in Norwegian aquaculture. Sea lice infestation may cause skin lesions and subsequent osmo-regulatory problems, thereby subjecting the fish to secondary infections. Resistance to some sea lice agents has resulted in increased sales of other agents. Use of veterinary medicinal products for treatment of sea lice has been high since 2009.

An increasing use of flubenzurons has raised concerns over its possible environmental dissemination and impacts. In short, sea lice belong to the crustacean group, and flubenzurons from aquaculture may be expected to influence other crustacean species near the treated fish cages (Samuelsen et al., 2014). Crustaceans, shellfish and wild fish near cages receiving treatments may obtain flubenzurons from excess medicated feed pellets or from active substances in fish faeces. However, there is a ban to catch wild fish close to farming sites, and data show that the risk of exceeding acceptable daily intake (ADI) of teflubenzuron (ADI = 0.01 mg/kg bw) from wild fish is neglectable (Samuelsen et al., 2013). However, this issue is beyond the scope of this opinion to comment on.

VMP against sea lice are included in surveillance programme on veterinary medicinal products in food in accordance with EU- Directive 96/23/EC, and no residues above the given MRL for the various VMPs has been detected (Hannisdal et al., 2014).

Other agents

As in 2006, several disinfectants and cleaning agents are approved for use in the food industry including the seafood industry. The risk from exposure to these substances from farmed fish is probably limited.

In aquaculture, prevention and treatment of fungal infections (*Saprolegnia* spp) are done by topical application of fungicides (veterinary medicinal product, VMP) to farmed fish and roe (only prevention). The use of the fungicide bronopol (a VMP), for bath treatment of fish has been relatively stable in the period 2010-2012, but increased by 30% in 2013.

Malachite green is no longer allowed for application in aquaculture. The regular surveillance programme has not detected malachite green in farmed fish.

2.3 Summary of reference values for selected nutrients and undesirable substances

The majority of health authorities worldwide recommend a regular fish intake in order to ensure proper nutrition and health benefits (Chapter 1).

Nutrients in fish

Several updates of recommendations for nutrients present in fish have been published.

- In 2010 EFSA established recommendations for intake of EPA and DHA
 - Adults: 250 mg/day for primary prevention of coronary heart diseases in healthy subjects
 - Pregnant and lactating women: Additional 100 to 200 mg DHA per day was recommended
 - Older infants (older than 6 months of age) and young children below the age of 24 months, an Adequate Intake of 100 mg DHA was proposed
 - Young children above 2 years: EFSA proposed that dietary advice for should be consistent with advice for the adult population (i.e., 1-2 fatty fish meals per week or ~125 mg of EPA and DHA per day when adjusted for portion size)
- In 2014, based on the Nordic Nutrition Recommendations 5th edition (2012), the Norwegian Directorate of Health revised the Norwegian recommendations. They:
 - established a new recommendation for DHA of 200 mg/day for pregnant and lactating women
 - increased the recommended intake of vitamin D from 7.5 µg to 10 µg/day for children above 2 years and adults, and to 20 µg/day for the elderly (75 or more years of age)

- increased the recommended intake of selenium from 50 µg to 60 µg/day for men and from 40 µg to 50 µg/day for women
- kept the recommendations for iodine intake unchanged

Contaminants in fish

- The substances mainly addressed in this opinion are methylmercury and dioxins and dl-PCBs because they occur in fish at levels that may result in exposure close to tolerable intakes. Other contaminants are also present in fish. Several of the compounds in the group of chlorine-, fluorine or bromine-substituted organic compounds, including dioxins and dl-PCBs, are declining in the environment because they are no longer in use.
- Fish is the only important dietary source of methylmercury. Since the VKM benefit risk assessment of fish consumption in 2006, a new tolerable intake for methylmercury has been set by EFSA which implicated a reduction from 1.6 to 1.3 µg/kg bw/week, expressed as mercury.
- For dioxins and dl-PCBs, the TWI established by SCF at 14 pg TE/kg bw/week in 2001 (SCF, 2001) is still valid.
- For ndl-PCBs, EFSA could not establish a tolerable intake because of difficulties in distinguishing effects of ndl-PCBs from those of dl-PCBs (EFSA, 2005). Since exposure to ndl-PCBs is normally highly correlated with exposure to dioxins and dl-PCBs, VKM concluded in 2008 that with the combination of dioxins and PCBs in Norwegian food, exposure to dioxins below the TWI would also protect against toxicological effects from exposure to ndl-PCBs (VKM, 2008).
- For PBDEs and HBCDs, EFSA concluded that the risk of adverse health effects from exposure is low (EFSA, 2011), but no tolerable intakes could be set. The margins between levels in Europeans and levels exerting toxicity in experimental animals was high, indicating low concern.
- For fluorinated substances, the TDIs set by EFSA in 2008 for PFOS and PFOA are orders of magnitude higher than the dietary exposure in Norway.

Medicine residues in farmed fish

- When farmed fish is medicated, several measures are taken to ensure food safety for the consumer. These include retention times after treatment and large programs to control that the maximal residue limits (MRL) for veterinary medicinal products are not exceeded in farmed fish.
- No residues of banned substances or medicine residues above EU maximal residue limits for veterinary medicinal products have been detected in any of the analysed 30 000 samples from farmed fish (1998-2013). The residues controlled include e.g. antibiotics and agents against sea lice.

The reference values used by VKM as basis for benefit and risk characterization of nutrient intake and contaminant exposures from fish in the present opinion are shown in Tables 2.3-1 and 2.3-1.

Table 2.3-1 Recommended daily intakes for nutrients used for benefit and risk characterisation (Chapter 8)

Population groups	Recommended intakes for nutrients			
	EPA+DHA mg/day	Vitamin D ^c µg/day	Iodine ^c µg/day	Selenium ^c µg/day
2-year- olds	~125 ^a	10	90	25
Adults	~250 ^b	10 (20) ^d	150	50 (women) 60 (men)
Pregnant women	~250 (+100-200 DHA) ^b 200 DHA ^c	10	175	60

^aaccording to EFSA (2010b) and adjusted for portion size for children being 50% of an adult portion of 150 g

^baccording to EFSA (2010b)

^caccording to Norwegian dietary recommendations (Norwegian Directorate of Health, 2014), which were based on the Nordic Nutrition Recommendations 5th edition (NNR5, 2012)

^dFor elderly (>74 years), vitamin D is recommended at 20 µg/day

Table 2.3-2 Tolerable weekly intakes for contaminants used for benefit and risk characterisation (Chapter 8)

Population groups	Tolerable weekly intake for contaminants	
	Methylmercury ^a µg/kg bw/week	Sum dioxins and dl-PCBs ^b pg TEQ/kg bw/week
2-year-olds	1.3	14
Adults	1.3	14
Pregnant women	1.3	14

^aaccording to EFSA (2012a)

^baccording to SCF (2001)

3 Fish and fish products in the Norwegian diet

Norwegians have traditionally had a relatively high fish and seafood consumption, especially in the coastal areas. Fishing and hobby angling contribute to higher fish consumption in subgroups of the population. The previous report (VKM, 2006) provided an overview of how to assess information about fish consumption and methodological challenges when assessing information about fish consumption. In the 2006 report (VKM, 2006), information about fish consumption was derived from dietary studies available at the time. These were the Norkost 1997 (adults), Spedkost 1998-99 (infants 6 months and 1-year-olds), Småbarnskost 1999 (2-year-olds), and Ungkost 2000 (4-, 9- and 13-year-olds). In addition, data from the Norwegian Fish and Game study, a national survey of the consumption frequencies relating to specific foods considered to contain potentially high levels of environmental contaminants, was included, and also some preliminary results from the Norwegian Mother and Child Cohort Study (MoBa) were presented.

In this report we have used information about fish consumption from newer national dietary surveys in 2-year-olds (Småbarnskost 2007) and adults (Norkost 3) as well as information about fish consumption reported during the time period 2002-2008 by pregnant women in MoBa.

Data from the national food consumption survey Ungkost 2000, with food consumption data for the age groups 4-, 9-, and 13-year-olds were considered too old to be used in this opinion. It is not known to which extent the fish consumption patterns have changed, neither in amount consumed nor type of fish eaten, in these age groups.

3.1 Description of food consumption surveys

The estimated consumptions of fish presented in this opinion are based on data from the national food consumption surveys for children (2-year-olds), adults (18-70-years) and from the MoBa cohort for pregnant women. The food consumption data from the three studies used in this opinion are the most complete and detailed data currently available in Norway.

However, it should be pointed out that three different methodologies were used in the different surveys and thus direct comparisons between the different study populations (2-year-old children, adults, pregnant women) can be misleading.

A description of the food consumption surveys and the different methodologies used is given below:

Two-year-olds: Småbarnskost 2007 is part of the national dietary surveillance system. The study was conducted by the University of Oslo, and financed by the Norwegian Directorate of

Health and the NSFA. Småbarnskost 2007 is based on a semi-quantitative food frequency questionnaire (FFQ). Ten questions in the FFQ asked about fish intake. In addition to predefined household units, food amounts were also estimated from photographs. The study was conducted in 2007, and a total of 1674 2-year-olds participated (participation rate 56%) (Kristiansen et al., 2009).

Adults: Norkost 3 is part of the national dietary surveillance system. The study was conducted by the University of Oslo, and financed by the Norwegian Directorate of Health and the NSFA. Norkost 3 is based on two 24-hour recalls by telephone at least one month apart. Food amounts were presented in household measures or estimated from photographs (Totland et al., 2012). The study was conducted in 2010/2011 and 1787 men and women aged 18-70 years participated (participation rate 37%). A total of 97 different fish and fish containing foods were reported in the two 24-hour recalls. The participants were asked to fill in a food propensity questionnaire after having completed the two 24-hour recalls. A total of 1453 participants filled in the questionnaire. The propensity questionnaire consists of 216 frequency questions of different foods, drinks, dishes and supplements. Of these, 21 questions asked about fish consumption and there were three questions about fish- and cod liver oil.

In Småbarnskost 2007 and Norkost 3, the daily intake of nutrients and exposure to contaminants of fish and fish products was computed by using food databases in the software system (KBS – "kostberegningssystem") developed at the Institute of Basic Medical Sciences, Department of Nutrition, at the University of Oslo. The food databases are mainly based on various versions of the official Norwegian food composition table (Rimestad et al., 2000) and are continuously supplemented with data on new food items.

Pregnant women (MoBa): The Norwegian Mother and Child Cohort Study (MoBa) is a prospective population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health (Magnus et al., 2006). Participants were recruited from all over Norway from 1999 to 2008. The women consented to participation in 40.6% of the pregnancies. The cohort now includes 114500 children, 95200 mothers and 75200 fathers. An FFQ was developed and validated specifically for this cohort (Brantsaeter et al., 2008; Meltzer et al., 2008). This FFQ was used from February 2002 and onwards. The current opinion included dietary reports from 86277 pregnancies. Thus, estimation of nutrient intakes has been based on all 86277 participants, while exposure to contaminants has been based on 83782 participants because body weights were not reported for 2494. The MoBa FFQ is a semi-quantitative questionnaire designed to capture information on dietary habits during the first 4-5 months of pregnancy. Frequencies were converted into food amounts using portion sizes for women and FoodCalc (Lauritsen, 2005), and women with improbable energy intakes were excluded (1.6%), i.e. energy intake below 4.5 MJ or above 20 MJ.

3.2 The consumption of fish and fish products in Norwegian dietary surveys

The fish consumption is presented as raw fish to match the concentration data of nutrients and contaminants analysed in raw fish. Details regarding percentages of raw fish content in various fish products and type of fish used for each fish product are presented in Appendix I. The exception is cod roe and liver pâté, in which concentration data for nutrients and contaminants was analysed from the whole product, and not divided into cod roe, cod liver and cod liver oil.

The Norwegian and Latin names for various fish species are listed in Appendix II.

3.2.1 Two-year-olds

Table 3.2.1-1 shows the number of consumers and consumption of different fish species and fish product categories in the 2-year-olds. Nearly all the 2-year-olds, 98%, reported eating fish, but the distribution of which type of fish and amounts of consumption differed widely. The 10 questions in the FFQ about fish intake covered fish balls/fish pudding, fish au gratin, fish burgers, fish fingers, cod/saithe, trout/salmon, cod roe and liver pate, mackerel in tomato-sauce, caviar, and jarred baby food with fish.

Table 3.2.1-1 Consumption of raw fish in 2-year-olds (Småbarnskost 2007, n=1674)

Food item	Number of consumers		All participants (n=1674)		
	n	%	Mean g/day	Median g/day	P95 g/day
Fish, total	1640	98	16	14	36
Lean fish (≤5% fat)	1609	96	10	9	24
Atlantic cod/saithe, filet ^a	1158	69	2	1	6
Fish balls, fish pudding ^a	1243	74	3	2	9
Fish au gratin ^a	1040	62	1	<1	3
Fish burgers ^a	1196	71	3	2	8
Fish fingers ^a	940	56	2	1	6
Jarred baby food w/fish ^a	68	4	<1	0 ^b	<1
Fatty fish (>5% fat)	1238	74	5	2	16
Salmon (farmed)	1013	61	1	1	4
Mackerel in tomato sauce ^a	736	44	3	0 ^b	14
Fish roe and liver	697	42	1	0 ^b	5
Cod roe and liver pâté	54	3	<1	0 ^b	- ^c
Roe (in caviar)	685	41	1	0 ^b	4

P95 = 95th percentile

^aOnly raw fish content from the different food products are included.

^bMedian is zero due to less than 50% of the participants eating the fish or fish product.

^cLess than 60 consumers

The mean consumption of fish per day was 16 g, median consumption was 14 g and high (95th percentile) consumption was 36 g of fish per day. Lean fish contributed with 63% of the total fish consumption, fatty fish contributed 31% and cod roe and liver contributed 6%. Fish products like fish cakes and fish balls/pudding were the foods that contributed most to lean fish intake, while mackerel from mackerel in tomato-sauce was the most eaten fatty fish.

Cod as filet and in fish products was reported eaten by 96% of the participants. Farmed salmon was most often reported of the fatty fishes, with 61% consumers. Fish as bread spread was frequently reported, and 44% of the participants used mackerel in tomato-sauce as bread spread, and also caviar was used by 41% of the participants. Cod roe and liver pate was only reported eaten by 54 of the participants.

Consumption of fish oils and cod liver oil in 2-year-olds

Mean consumption of fish/cod liver oil was 2 g/day in 2-year-olds, while the 95th percentile was 6 g/day (Table 3.2.1-2). A total of 41% of the 2-year-olds were given fish/cod liver oil (Table 3.2.1-3). The 2-year-olds that were given fish/cod liver oil as a supplement had a significantly higher mean fish intake (18 g/day) than those who were not given such supplement (15 g/day).

Table 3.2.1-2 Consumption of fish oil and cod liver oil in 2-year-olds (Småbarnskost, n=1674)

Supplement	All participants	
	Mean g/day	P95 g/day
Fish oil/cod liver oil	2	6

P95 = 95th percentile

Median is not given, but was zero because less than 50% of the participants had consumed fish oil or cod liver oil.

Table 3.2.1-3 Consumption of fish oil and cod liver oil in 2-year-olds in consumers only (Småbarnskost 2007, n=689)

Supplement	Number of consumers		Consumers only		
	n	% of 1674	Mean g/day	Median g/day	P95 g/day
Fish oil/cod liver oil	689	41	4	5	6

P95 = 95th percentile

3.2.2 Adults

Table 3.2.2-1 presents the mean consumption of the different fish and fish categories for all participants and how many of the participants in Norkost 3 that consumed fish and different fish categories during the two 24-hour recalls.

A total of 97 different fish and fish containing foods were reported in the two 24-hour recalls. Only the content of raw fish is presented from the fish products, except for cod roe and liver pâté.

When only two days of food intake are the basis for the fish consumption, persons that have eaten fish for dinner on both recall-days will be represented in the 95th percentile. It is unlikely that even a high fish consumer eats fish every day for a prolonged time, and therefore, the high mean fish consumption among those who reported fish for dinner both of the two consumption days represents an overestimate. Also, many participants with no registered fish intake during the two 24-hour recalls will usually eat fish. A total of 61% of the participants in the two 24-hour recalls had eaten fish, while 97% of the participants had reported to eat fish at least once a month in an accompanying questionnaire (Chapter 3.2.2.1). This leads to a low median intake, and for fish species the median will be zero because less than 50% of the participants have eaten the specific fish during the two 24-hour recalls. VKM has therefore not included the median for the adult population in the tables, but the median for total fish consumption is cited in the text.

Table 3.2.2-1 Consumption of raw fish in adults (Norkost 3, n=1787)

Food item	Number of consumers		All participants	
	n	%	Mean g/day	P95 g/day
Fish, total	1095	61	52	201
Lean fish (≤5% fat)	577	32	30	162
Saithe	69	4	3	<1
Atlantic cod	468	26	24	141
Haddock	10	1	<1	_ ^a
Redfish	8	<1	1	_ ^a
Wolffish	4	<1	<1	_ ^a
Plaice	12	1	<1	_ ^a
Tuna	49	3	2	_ ^a
Fatty fish (>5% fat)	648	36	21	113
Herring (Norwegian spring spawning)	99	6	1	9
Halibut	15	1	1	_ ^a
Mackerel	257	14	4	30
Salmon (wild)	6	<1	< 1	_ ^a
Salmon (farmed)	323	18	12	83
Trout (freshwater)	4	<1	< 1	_ ^a
Trout (farmed)	28	2	1	_ ^a
Fish roe and liver	248	14	1	7
Cod roe	237	13	1	5
Cod roe and liver pate	18	1	<1	_ ^a
Cod liver	3	<1	<1	_ ^a
Fish from fish products^b	243	14	7	51
Fish as bread spread^b	636	36	9	51

P95 = 95th percentile.

^aNo 95th percentile due to less than 60 consumers.

^bFish from fish products and bread spread are also a part of the lean and fatty fish categories.

The mean consumption of fish per day was 52 g, while the 95th percentile participant reported to consume 201 g of fish per day. The median intake for total fish was 17 g. Lean fish contributed most with 60% of the total fish consumption, while fatty fish contributed 40%. Cod was the most consumed fish category, and was eaten both as filet and as ingredient in fish products. Fish from fish products contributed with approximately 30% of the fish consumption. Farmed salmon was the most eaten fatty fish.

Fish consumption differs with gender, and in this study sample, the daily mean and high intakes (95th percentile) were 44 g (175 g) in women and 62 g (239 g) in men. Using the average will lead to an underestimation of nutrient intakes from fish in men and an overestimation of nutrient intakes in women. However, for contaminant exposures this will be evened out as exposure estimates are divided by body weight. VKM decided to use the average for both men and women. The proportion of lean and fatty fish was comparable in men and women.

Consumption of fish oils and cod liver oil in adults

Mean consumption of fish oil/cod liver oil was 3 g/day in adults, while the 95th percentile was 10 g/day (Table 3.2.2-2). There were 25% of the participants who reported taking fish oil/cod liver oil, measured in spoons, while 17% reported to have taken one or several capsules with fish oil. A total of 37% of the adults reported to take fish oil/cod liver oil during the two 24-hour recalls (Table 3.2.2-3). The adults that took fish oil/cod liver oil as a supplement had a mean fish intake of 56 g/day, while those not reporting taking fish oil/cod liver oil had a mean fish intake of 50 g/day. There was a significant difference in fish consumption between those who reported taking fish oil/cod liver oil, and those who did not take fish oil/cod liver oil.

Table 3.2.2-2 Consumption of fish oil and cod liver oil in adults (Norkost 3, n=1787)

Supplement	All participants	
	Mean g/day	P95 g/day
Fish oil/cod liver oil, n=1787	3	10

P95 = 95th percentile

Median is not given, but was zero because less than 50% of the participants had consumed fish oil and cod liver oil.

Table 3.2.2-3 Consumption of fish oil and cod liver oil in adults, consumers only (Norkost 3, n=663) for each type of fish oil

Supplement	Number of consumers		Consumers only		
	n	% of 1787	Mean g/day	Median g/day	P95 g/day
Fish oil/cod liver oil, n=663	663	37	7	2	11

P95 = 95th percentile.

3.2.2.1 Food propensity questionnaire

In Norkost 3 (Totland et al., 2012), the participants were asked to fill in a food propensity questionnaire after having completed the two 24-hour recalls. A total of 1453 out of 1787 participants filled in the questionnaire. The propensity questionnaire consisted of 216 frequency questions of different foods, drinks, dishes and supplements. Of these, 21 questions were asked about fish consumption and three about fish- and cod liver oil. Some of the questions were aggregated, and are therefore not possible to directly compare with the more specific data from the two 24-hour recalls. Examples of aggregated question in the propensity questionnaire are: "Fish casserole, fish soup and fish au gratin" and "Fish/shellfish in wok, salad i.e."

Comparison of the percentages of fish consumers measured with the two assessment methods; two 24-hour recall (Table 3.2.2-1) and propensity questionnaire (Table 3.2.2.2-1), shows that the percentage of fish consumers is lower in all categories in the two 24-hour recalls.

Table 3.2.2.2-1 Fish consumers (%) measured with food propensity questionnaire, and frequencies per day of each fish category or fish product (n=1453)

Food item	Food propensity questionnaire		
	% fish consumers (n=1453)	Mean	Frequency per day P95
Fish, total, n=1453	97	0.80	2.19
Lean fish (≤ 5% fat)			
Cod, saithe, haddock (boiled/fried)	62	0.08	0.22
Wolffish, redfish (boiled/fried)	18	0.02	0.08
Fatty fish (> 5% fat)			
Halibut (boiled/fried)	11	0.01	0.03
Herring (boiled/fried/salted/smoked)	8	0.01	0.03
Mackerel (boiled/fried/smoked)	9	0.01	0.03
Wild salmon or trout (boiled/fried)	18	0.02	0.08
Farmed salmon or trout (boiled/fried)	54	0.06	0.22
Fish products			
Fish cakes, fish pudding, fish balls etc ^b	62	0.06	0.15
Breaded fish (fish fingers, stuffed plaice etc.)	36	0.03	0.08
Fish casserole, fish soup, fish au gratin	56	0.05	0.15
Fish/shellfish in wok, salads etc.	31	0.03	0.15
Sushi	14	0.01	0.08
Sandwich spreads from fish			
Caviar (based on cod roe)	53	0.13	0.64
Cod roe and liver pate	10	0.02	0.10
Mackerel fillet in tomato sauce	67	0.19	0.64
Smoked/cured salmon	55	0.08	0.36
Sardines, pickled herring, anchovies	35	0.06	0.36
Tuna (canned)	24	0.03	0.14
Other (fish pudding, fish balls etc.)	48		- ^c
Freshwater fish			
Freshwater fish, e.g pike, perch	4	0.01	0.2
Fish liver (cod, saithe)	2	<0.01	0.01

P95 = 95th percentile

^aFish consumer defined as reported eating the fish product at least once a month

^bFish cakes, fish pudding, fish balls etc. are presented here due to difficulties in separating fish cakes eaten as bread spread or for dinner in the two 24-hour recalls.

^cFish cakes, fish pudding, fish balls etc. are presented as fish products, and not as bread spread.

There were significant differences in total fish consumption between those who had filled in the propensity questionnaire and those who did not ($p=0.02$). Those who filled in the propensity questionnaire reported eating more fish than those who did not fill in the questionnaire (median 18 g vs. 5 g fish per day).

Contrary to what was seen for fish consumption, use of fish oil/cod liver oil supplements did not differ much between the two assessment methods (Table 3.2.2.2-2). A likely explanation is that persons using dietary supplements tend to do this on a daily basis.

Table 3.2.2.2-2 Percentage of fish oil and cod liver oil supplement users according to the food propensity questionnaire (n=1453) and two 24-hour recalls (n=1787)

Supplement	Food propensity questionnaire % consumers ^a (n=1453)	Two 24-hour recalls % consumers (n=1787)
Fish oil/cod liver oil, total	32	37

^aSupplement consumer is defined as taking the fish oil and cod liver oil at least once per week.

^bSupplement consumer is defined as taking the fish oil and cod liver oil at least once during the two 24-hour recalls.

3.2.3 Pregnant women

Fish consumption in pregnant women in MoBa is described in Table 3.2.3-1. Fish consumption was assessed using a food frequency questionnaire (FFQ) and represents the average habitual intake during the first half of pregnancy. The FFQ included 8 questions about cold cuts and spreads made of fish or shellfish, 13 questions about fish or shellfish eaten for dinner, and four questions about cod liver oil, cod liver oil capsules or fish oil capsules.

Table 3.2.3-1 Consumption of fish in pregnant women (MoBa, n=86277)

Food item	Number of consumers		All participants (n=86277)		
	n	%	Mean g/day	Median g/day	P95 g/day
Fish, total	83848	97	31	27	68
Lean fish (\leq 5% fat)	80926	94	18	16	41
Atlantic cod, saithe, haddock	77895	93	15	13	35
Redfish, catfish	23283	27	1	0	7
Pike, perch	1231	1	<1	0 ^a	<1
Tuna	16945	18	1	0 ^a	5
Halibut, flatfish	21093	24	1	0 ^a	4
Fatty fish ($>$ 5% fat)	75319	87	11	7	36
Mackerel, herring	59184	69	6	2	28

Food item	Number of consumers		All participants (n=86277)		
	n	%	Mean g/day	Median g/day	P95 g/day
Salmon, trout	66286	77	5	4	15
Fish roe and liver	41215	48	2	0 ^a	8
Fish liver	918	1	<1	0 ^a	<1
Cod roe and liver pate	3761	4	<1	0 ^a	<1
Roe	40162	47	2	0 ^a	8

P95 = 95th percentile

^aMedian is zero due to less than 50% of the participants eating the fish or fish product.

Nearly all the women reported fish intake (97%) and for total fish consumption the mean and 95th percentile did not differ between all and consumers only. The average total fish intake was 31 g/day (corresponding to 217 g/week), median intake was 27 g, and high consumption was 68 g/day. Lean fish consumption was reported by 94% and fatty fish by 87% of the women. Lean fish constituted the largest part of total fish, with 18 g/day (60%), fatty fish contributed 11 g/day (37%), corresponding to ratio of 2/3 lean and 1/3 fatty fish. Fish liver and roe constituted a small part of total fish consumption.

The consumption of fish oils and cod liver oil in pregnant women

Fish oil and cod liver oil supplements were the most frequently used supplements reported by pregnant women in MoBa (Haugen et al., 2008). In 40108 women recruited during years 2002 to 2005, fish oil and cod liver oil supplements were used by 59%, and 19% used more than one brand of n-3 supplement. In all women in MoBa (n=86277), which are included in the current report, use of fish oil and cod liver oil supplements was reported by 68%, with an increasing prevalence of fish oil and cod liver oil supplement use from 2002 to 2009 (Table 3.2.3-2)

Table 3.2.3-2 Use of fish oil and cod liver oil supplements in pregnant women (MoBa, n=86277) by year

Year	% pregnant women (n=86277) using fish oil/cod liver oil supplement
2002-2003	54
2004-2005	63
2006-2007	75
2008	77

Fish oil and cod liver oil supplement users had significantly higher fish intake than non-supplement users.

3.3 Previous estimates of fish consumption and changes in fish consumptions since 2006

In the 2006 report (VKM, 2006), information about fish consumption was derived from dietary studies available at the time. These were the Norkost 1997 (adults), Spedkost 1998-99 (infants 6 months and 1-year-olds), Småbarnskost 1999 (2-year-olds), and Ungkost 2000 (4-, 9- and 13-year-olds). In addition, data from the Norwegian Fish and Game study part A was extensively used, and also some preliminary results from the Norwegian Mother and Child Cohort Study (MoBa) were presented.

In order to address changes in fish consumption since 2006, the methods behind the dietary surveys used then and now have to be taken into consideration (Table 3.3-1).

The methods used (FFQ) in Småbarnskost 1999 and Småbarnskost 2007 were similar, and data from these two surveys can be compared even though the questions in the FFQs differ for some food groups. However, for adults, the methods used in the Norwegian Fish and Game study part A (FFQ) and Norkost 3 (two 24-hour recalls) are **not** similar, and data from these two surveys cannot be directly compared. However, both studies were nation-wide and participants were invited by arbitrary selection from the population.

Table 3.3-1 Overview of the different dietary studies used in the VKM benefit-risk assessment of fish in 2006 and in the present opinion

Study	Year	Number of participants		Dietary assessment method	Type of seafood addressed in VKM reports
		n	% participation rate		
2-year-olds					
Småbarnskost 1999 (Used by VKM in 2006)	1999	1720	57	Food frequency questionnaire	Fish Fish products Seafood
Småbarnskost 2007 (Used in the present opinion)	2007	1674	56	Food frequency questionnaire	Raw fish No seafood
Adults					
Fish and game study, part A (Used by VKM in 2006)	1999	6015	60	Food frequency questionnaire	Fish Fish products Seafood
Norkost 3 (Used in the present opinion)	2010/2011	1787	37	Two 24-hour recalls	Raw fish No seafood
Pregnant women					
MoBa (Used by VKM in 2006)	2002-2003	19138	~40	Food frequency questionnaire	Fish Fish products Seafood
MoBa (Used in the present opinion)	2002-2008	86277	~40	Food frequency questionnaire	Raw fish No seafood

University of Oslo (UiO) has conducted a calibration study where Norkost 3 and Norkost 1997 has been compared (A.M.W. Johansen et al., UiO, pers. comm.). The same persons have been interviewed both with the two 24-hour recalls used in Norkost 3 and filled in the food frequency questionnaire used in Norkost 1997 (n=240 men and women). For fish and fish products, the mean intake with the Norkost 3 two 24-hours recalls was 67 g/day (SD

95th g/day), and the mean intake with the Norkost 1997 FFQ was 74 g/day (SD 48 g/day) (A.M.W. Johansen et al., UiO, pers. comm.). The calibration study concluded that: "It is generally not advisable to conclude on changes in diet based on Norkost 1997 and Norkost 3." However, since the overall consumption in adults was within the same order of magnitude, VKM decided to use the mean consumption at group levels for approximate comparison of fish consumption in adults in 2006 and 2014 in the present opinion. Some methodological details on the dietary surveys used in VKM assessment from 2006 and in the present opinion are found in Appendix III.

3.3.1 Two year olds

In the VKM assessment from 2006 (VKM, 2006), fish consumption in 2-year-olds was based on food frequency data assessed in 1998-1999 in a nationally representative sample of 1720 2-year-old children. The mean intake reported in 2006 based on a survey in 1998-99 was 20 g/day, the median intake was 16 g/day and 95th percentile intake was 46 g/day. In the present report, the mean consumption in 2-year-olds is 16 g/day, the median is 14 g and the 95th percentile is 36 g/day. Both surveys (1998-99 and 2007) used FFQs, but the consumption data reported in VKM (2006) included shellfish and the full weight of fish products (not only the raw fish proportion), which explains the difference between the two time points. Hence, there is no indication of a change in fish consumption in 2-year-olds since 2006. (VKM, 2006) reported that lean fish contributed approximately 70% and fatty fish 20% of the total fish intake in 2-year-olds in 1999, while the corresponding figures in the current update is 63% and 31%. This may indicate a slight shift (about 10%) towards a lower proportion of lean fish relative to fatty fish.

(VKM, 2006) reported that 45% of the 2-year-olds were given cod liver oil in 1999, while in the current update 41% were given cod liver oil and fish oil, indicating a small reduction in supplement use in this age group. It is likely that fish oil and cod liver oil has been replaced by other supplements containing vitamin D.

In comparison to the VKM assessment from 2006 (VKM, 2006), the estimated total consumption of fish in 2-year-olds is basically unchanged.

3.3.2 Adults

Fish consumption data and estimated intake of nutrients and exposure to contaminants in (VKM, 2006) was based data assessed by a FFQ in the Fish and Game Study part A, a nationally representative sample comprising 6015 men and women aged 18-79 year was included (Meltzer and Stigum, 2002). The Fish and Game study included other seafood (e.g. shellfish) and not only fish as in the current update. A direct comparison with the current estimates of fish consumption is not possible and has not been tabulated. However, comparison of "fish and other seafood" consumption (and not just "fish") shows that the mean consumption of "fish and other seafood" which in the VKM assessment from 2006 (VKM, 2006) was 70 g/day (65 g in women and 75 in men) is similar to the mean

consumption of "fish and other seafood" presented in the Norkost 3 report (Totland et al., 2012), which is 67 g per person per day (56 g in women and 79 g in men). The pattern of adult fish consumption in (VKM, 2006) showed that lean and medium fatty fish (less than 5% fat) comprised nearly 2/3 of the total fish intake. Hence, there is no indication of a change in fish consumption at the individual level since 2006. This is supported by Norwegian food supply statistics. These statistics are prepared on an annual basis at the request of the Directorate for Health and Social Affairs and show that the sale of fish and fish-products has remained stable from 2006 to 2013 (Norwegian Directorate of Health, 2013).

3.3.3 Pregnant women

The VKM assessment from 2006 (VKM, 2006) presented data on fish and seafood consumption based on the women recruited in 2002 and 2003, with an estimated average daily intake of 46 g total seafood per day. This figure is higher than the estimated average daily intake in this update (31 g/day). However, the figure used in 2006 included shellfish and the full weight of composite fish dishes is therefore not comparable to the current estimate which only includes the fish-part of composite fish-dishes.

In a study within MoBa focusing on maternal dietary exposure to dioxins and PCBs during the time period 2002 to 2008, Caspersen et al. (2013) reported that during this time period the total median consumption of fish and seafood remained stable around 31 g/day. However, the median consumption of lean fish (less than 2% fat) decreased from 15.8 g/day in 2002–2003 to 13.7 g/day, while simultaneously, there was a small increase in consumption of medium fatty (2-8% fat) fish (from 1.9 to 2.9 g/day) and salmon/trout (from 1.9 to 2.9 g/day) (Caspersen et al., 2013).

The quantitative figure for fish consumption in pregnant women used by VKM (2006) is not comparable to newer estimates as the former included shellfish and the full weight of all ingredients in composite fish dishes. Fish intake in MoBa reported by year of delivery showed stable low fish consumption from 2002 to 2008, but with a slight decrease in lean fish accompanied by a slight increase in medium-fatty and fatty fish. Use of fish oil and cod liver oil supplements increased from 59% in 2002-2005 to 77% in 2008.

3.4 Summary of consumption of fish and fish products in Norwegian dietary surveys

In this updated report we have used information about fish consumption from newer national dietary surveys in 2-year-olds (Småbarnskost 2007) and adults (Norkost 3, 2010/2011) as well as information for pregnant women who answered the MoBa FFQ (2002-2008). The distribution of lean fish and fatty fish (roe and liver included) is about similar in the three population groups, as lean fish contribute with 60% and fatty fish contribute with

approximately 40% to the total (Figure 3.4-1). The mean consumption expressed as g/day is however different in the three groups (Figure 3.4-2).

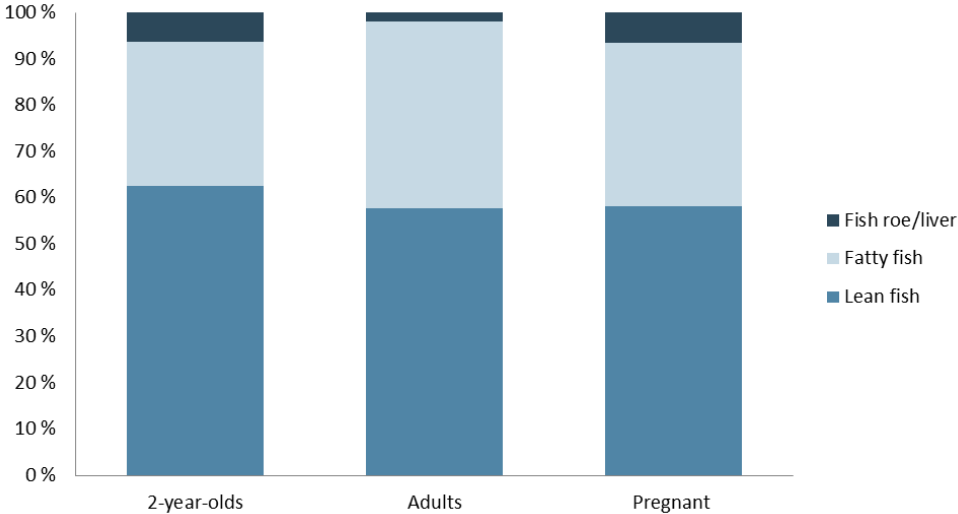


Figure 3.4-1 Mean distribution of lean and fatty fish consumption (% of total) in 2-year-olds, adults and pregnant women, respectively, based on the Småbarnskost 2007, Norkost 3 and MoBa. The figures are given in percentage of total raw fish consumption including proportion raw fish in fish products and bread spread.

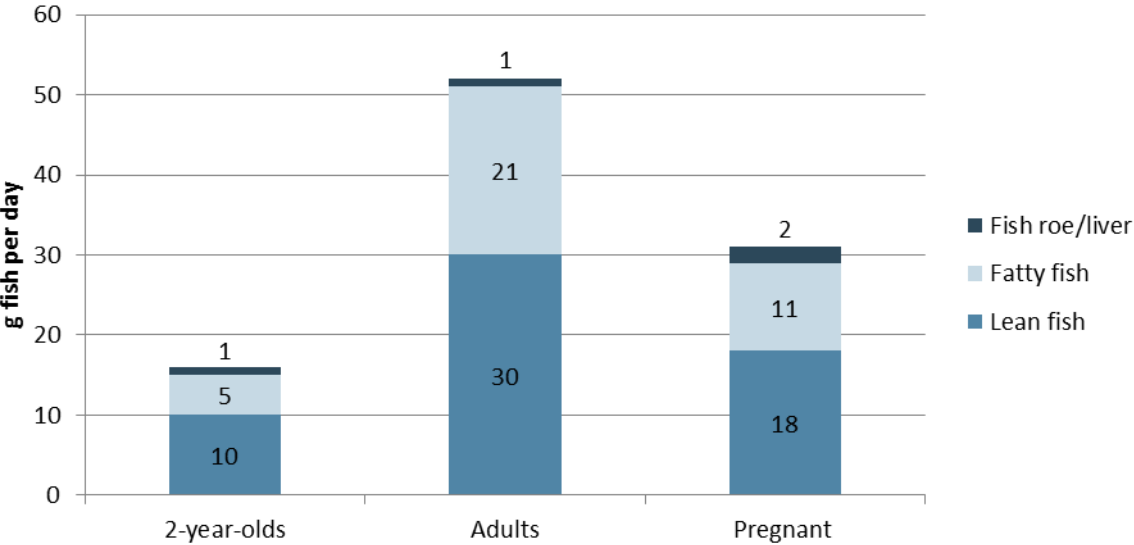


Figure 3.4-2 Mean fish consumption (g/day) given as raw fish including proportion raw fish in fish products and bread spread in 2-year-olds, adults and pregnant women, based on Småbarnskost 2007, Norkost 3 and MoBa, respectively. The distribution between lean fish, fatty fish and fish roe/liver is indicated.

Consumption data in the current update and comparison to VKM 2006 show that:

- For the 2-year-olds, fish intake was assessed with comparable instruments (FFQ) in the current update and in (VKM, 2006), but differences in estimation of total fish resulted in lower intake estimates in the present report.
 - The mean consumption of fish in 2-year-olds is 16 g/day, the median is 14 g and the 95th percentile consumption is 36 g/day.
 - The estimated total consumption of fish in 2-year-olds is relatively unchanged since 2006.
- For adults, fish intake was assessed with different dietary instruments in the current update than in (VKM, 2006). In addition, consumption data in (VKM, 2006) included both fish and other seafood, and differences in estimation of total fish intake.
 - The mean consumption of fish per day in adults is 52 g, the median is 17 g and the 95th percentile consumption is 201 g/day.
 - The consumption of fish in the Norwegian Fish and Game Study part A is not directly comparable with the Norkost 3 fish consumption. However, the mean consumption in the Norwegian Fish and Game study and Norkost 3 appear to be about similar.
- For pregnant women, fish intake was estimated with the MoBa FFQ both in the current update and in (VKM, 2006) but consumption data presented in (VKM, 2006) cannot be compared directly with the current estimate due to differences in estimation of total fish.
 - The mean consumption of fish in pregnant women is 31 g/day, the median is 27 g and the 95th percentile consumption is 68 g/day.
 - Fish intake in MoBa reported by year of delivery showed stable fish consumption from 2002 to 2008, but with a slight decrease in lean fish accompanied by a slight increase in fatty fish.

The fish consumption in 2-year-olds (Småbarnskost 2007), adults (Norkost 3) and pregnant women (MoBa, 2014) will be the basis for the intake and exposure assessment of nutrients and contaminants, respectively, in Chapter 7. Additionally, VKM has made various scenarios to foresee how possible changes in fish consumption pattern and amounts will affect the contribution from fish to recommended intakes of specific important nutrients, as well as to tolerable weekly intakes (TWI) of mercury, dioxins and dl-PCBs (Chapter 8).

4 Health effects associated with fish consumption – epidemiological studies

The VKM benefit-risk assessment of fish consumption in 2006 (VKM, 2006), investigated the following clinical health outcomes: cardiovascular disease, cancer, growth and development of the foetus and infants as well as allergies against fish and fish products. At the time there were no quantitative data available from individual studies that had concurrently assessed the negative effects of contaminants in relation to the positive effects of different nutrients. Thus, based on a qualitative assessment of existing literature (up to 2006) of epidemiological studies, VKM concluded that consumption of fish, lean or fatty, (three fish meals á 200 g/week; 2/3 lean and 1/3 fatty fish), has a positive overall health effect mainly due to the effects of fish consumption on cardiovascular disease and mortality. Furthermore, it appeared that intake of marine n-3 fatty acids from fish have a positive impact on length of pregnancy and foetal development.

Since 2006, large prospective studies have been conducted, assessing fish consumption and association with several different health outcomes. Furthermore, national and international expert organs have assessed risks and benefits associated with fish consumption as such, as well as nutrients from fish consumption and contaminants from fish consumption. These are introduced in chronological order below, but findings and conclusions from these assessments are referred when relevant under each health outcome (Chapters 4.7.1 – 4.7.5).

In January 2010, FAO and WHO held an expert consultation on the risks and benefits of fish consumption to review data on levels of nutrients (long-chain n-3 fatty acids) and specific chemical contaminants (methylmercury and dioxins) in a range of fish species in order to compare the health benefits of fish consumption and nutrient intake with the health risks associated with contaminants present in fish (FAO/WHO, 2011). In the FAO/WHO report, the literature on benefits of fish consumption for optimal neurodevelopment and cardiovascular disease, as well the risks from consuming fish containing methylmercury and dioxins (including PCBs) were systematically reviewed.

In 2011, the Norwegian National Council for Nutrition published their dietary advice to promote public health and prevent chronic diseases (Norwegian National Council for Nutrition, 2011). In this report a systematic literature review of fish consumption and various health outcomes (cardiovascular disease, cancer, type-2 diabetes, cognitive and visual development, mental health, psoriasis and rheumatoid arthritis, allergy, osteoporosis, adverse health effect of contaminants in fish, foetal developmental, obesity and overweight) were assessed.

Both the abovementioned systematic literature reviews used the system developed by the 2007 World Cancer Research Fund (WCRF) report (WCRF, 2007) for grading the evidence for fish consumption - health outcomes associations. The basic criteria for grading of evidence are given in (WCRF, 2007) "Food, nutrition, physical activity and the prevention of cancer: a global perspective", in Box 3.8). The modified use of these criteria are given by FAO/WHO (2011) and the Norwegian National Council for Nutrition (2011). Evidence was classified as convincing, probable, limited suggestive, and limited – no conclusion depending on the number and quality of supporting, non-supporting and contradicting studies.

Table 4.1 Short description of the terms used for grading of evidence (WCRF, 2007)

Term	Grade	Evidence is
Convincing	High	Strong enough to support a judgement of a convincing causal relationship, which justifies goals and recommendations designed to reduce the incidence of cancer
Probable	Moderate	Strong enough to support a judgement of a probable causal relationship, which would generally justify goals and recommendations designed to reduce the incidence of cancer
Limitid – suggestive	Low	Too limited to permit a probable or convincing causal judgement, but suggestive of a direction of effect
Limited – no conclusion	Insufficient	Too limited to permit a firm conclusion to be made

EFSA delivered in 2012 an opinion on the risks to human health related to the presence of inorganic mercury and methylmercury in food (EFSA, 2012a), addressing several health outcomes including cardiac disease and neurodevelopment (the derived tolerable intakes are referred in Chapter 2.4.1).

In May 2014, the US Food and Drug Administration published a quantitative assessment of the net effect on foetal neurodevelopment from eating commercial fish (as measured by IQ and also by early age verbal development in children) (FDA, 2014). Methylmercury was the contaminant addressed in this report.

Also recently, in June, 2014, EFSA published a Scientific Opinion on health benefits of seafood consumption (EFSA, 2014b). They focused on the beneficial effects of seafood consumption during pregnancy in relation to functional outcomes of children's neurodevelopment, and the effects of seafood consumption on cardiovascular disease risk in adults. They also addressed which nutrients in seafood may contribute to the beneficial effects of seafood consumption in relation to the above-mentioned outcomes and considered whether the beneficial effects of seafood consumption in relation to the above-mentioned outcomes could be quantified. Later EFSA will see the beneficial effects of seafood consumption in relation with the health risks associated with methylmercury exposure.

In this updating of the VKM 2006 benefit-risk assessment, results from the above mentioned assessments which are made by national and international health authorities and published before 2013 formed the background basis for the literature searched performed by VKM (Chapter 4.1). VKM has not systematically assessed reviews/meta-analyses nor individual studies for weight of evidence, but merely summarised the studies retrieved from the

literature search. It was considered being beyond the scope of this assessment to review individual studies included in reviews/meta-analyses.

In the following, for each health outcome, relevant results from these reports are initially summarised followed by brief summaries of other relevant meta-analyses, literature reviews and cohort studies retrieved from systematic searches for literature published after 2010. Some of the studies resulting from the literature search are also included in the assessments from FDA (2014) and EFSA (2014b), however, the main findings in these reports are also summarised in the beginning of each chapter when relevant.

Furthermore, specifically for the reduction of coronary heart disease (CHD) (Chapter 4.2) VKM has also reviewed studies which have explored the relationship between marine n-3 fatty acids and cardiovascular outcomes even if they have not reported on fish consumption. This was done because above mentioned reviews have taken into account that convincing evidence exist for an effect of marine n-3 fatty acids on the reduction of CHD. Such studies are also addressed by the VKM report from 2011 which evaluated negative and positive human health effects from intake of n-3 fatty acids from food supplements and fortified foods (VKM, 2011b).

4.1 Literature searches for fish consumption and marine n-3 PUFA

Two separate literature searches were conducted in order to assess new knowledge about benefit and risk of fish consumption. The main search aimed to retrieve studies addressing fish consumption and health outcomes. In addition, a secondary search was conducted aiming to identify whether new scientific evidence would imply a change in the previously established beneficial effects of supplementary EPA and/or DHA in prevention of cardiovascular diseases. A full evaluation of supplementary n-3 long-chain polyunsaturated fatty acids (n-3 LCPUFA) and all outcomes was beyond the scope of this update.

4.1.1 Search strategy fish consumption and health outcomes

In order to retrieve relevant publications addressing fish consumption and health outcomes, systematic literature searches in Medline and Embase were conducted. Both databases were used in order to ensure comprehensive study retrieval. The strategy for the searches was discussed within the project group and with a professional librarian who also performed the searches.

Initially, an explorative search was performed and thereafter the search set up was adjusted both to include more specific terms of salmon (e.g. Atlantic salmon) and to ensure a broader inclusion of systematic reviews and meta-analyses.

The main search included different terms for "fish", "consumption" and "health effects", as well as for the specific types of health outcomes (e.g. malignant, cancer). The terms of health outcomes were based on well-known end points concerning human health and fish

consumption and marine long-chain n-3 fatty acids (e.g. cardiovascular events, cancer, immunology, cognition), as well as on end points relevant for children and their development (e.g. infant birth weight, language development) in accordance with end points used in the VKM benefit and risk assessment of breastmilk for infant health in Norway from 2013. For view of the search terms used for the literature search done 11. April 2014, the reader is advised to Appendix IV.

The search period was limited to publications from 2009 to today due to the FAO/WHO report (FAO/WHO, 2011) which presents the systematic reviews and meta-analyses of fish consumption and health effects published until 2010. The search was further limited by omitting conference abstracts and set up to include publications written in English or Scandinavian languages (Danish, Swedish and Norwegian) only.

Based on the above described search strategy, the results from the main search were restricted to single studies published in 2014 in order to obtain studies not yet included in reviews and meta-analyses (restriction 1), or to systematic reviews and meta-analyses only (restriction 2), or geographically to Norway, Sweden, Iceland, Finland, and Denmark (restriction 3). The geographic restriction was chosen in order to retrieve studies based on data especially relevant for fish consumption in the Norwegian population

Additionally, a few studies not captured by the search but found in reference lists to the included studies or obtained by other means (hand searching) have been included.

4.1.2 Selection of epidemiological studies

The main study types for inclusion in this chapter were systematic reviews and meta-analyses of human fish consumption and the associated health outcomes, i.e. restriction 2. The criteria for inclusion were:

Fish or fish consumption in relation to health outcome was the main issue in the article.

Study population representative for the general population (e.g. not to specific patients groups) preferentially in the European Economic Area and North America.

Studies describing and/or comparing levels of nutrients or other bioactive compounds in various diets including fish were not included. We also excluded studies describing dietary practices including fish consumption in special patient groups. Studies of supplementary marine n-3 PUFA were excluded and handed over to the experts assessing studies on supplementary n-3. Additionally, position papers, conference abstracts/summaries, editorial comments and various dietary guidelines were excluded.

The main literature search identified 2460 articles. Restriction 1 resulted in 156 articles published in 2014. Restriction 2 resulted in 444 systematic reviews and meta-analyses and restriction 3 provided 163 articles from the Nordic countries. Duplicates between the various restrictions were eliminated.

Study titles were independently reviewed by two persons of the project according to the above mentioned inclusion criteria. Titles were selected if chosen of one of the experts. The abstracts from the selected titles were then again independently reviewed by two project group participants and full text studies were distributed in the project group for full text examination. A final total of 74 publications were identified and included in this chapter (Figure 4.1.2-1).

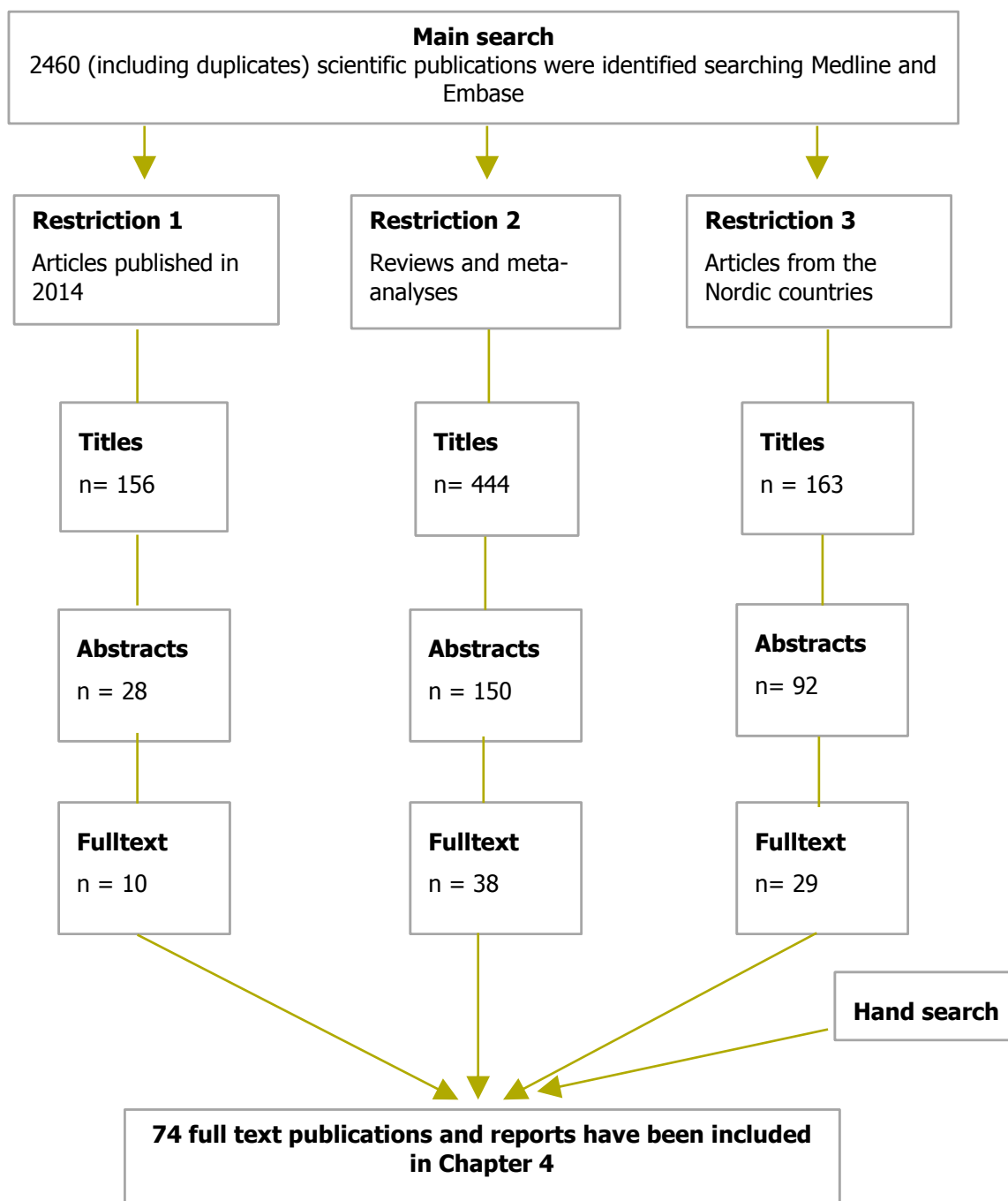


Figure 4.1.2-1 Flowchart for the literature search for fish consumption and associated health outcomes and the subsequent selection of publications.

4.1.3 Search strategy for supplementary n-3 fatty acids (EPA and/or DHA) and health outcomes

In order to elucidate additional aspects of fish consumption and health effects, a separate literature search aiming at supplementary n-3 fatty acids EPA and DHA and health effects was done. In 2011, VKM published an evaluation of negative and positive health effects of n-3 fatty acids as constituents of food supplements and fortified foods. The same search strategy as in the VKM report of 2011 was used, but the search period was limited from 2009. The search was performed 16. December 2013. The systematic literature search was conducted in Medline and Embase and aimed to retrieve systematic reviews and meta-analyses only, which were written in English, Norwegian, Danish or Swedish. For details, see Appendix V.

The search resulted in a total number of 733 abstracts which after removing of doublets left 559 references. Two experts read the abstracts, selected relevant articles and categorized these according to the outcome (cardiovascular, cancer, metabolic, immunologic, neurological and developmental). A full evaluation of all outcomes was considered beyond the scope of the current update. In the former VKM benefit and risk assessment of fish consumption (2006), the positive health effects of EPA and DHA, particularly on cardiovascular diseases, were included in the benefit part of the evaluation. The aim of the present update was therefore limited to identify whether new scientific evidence would imply a change in relation to the previously established beneficial effects of supplementary EPA and/or DHA in prevention of cardiovascular diseases.

Of the 559 references, 16 meta-analysis and systematic reviews addressing cardiovascular outcomes were selected for further evaluation. In addition, five meta-analyses that were not identified in the original literature search were included by hand-search. A total of six meta-analyses were selected to highlight and elaborate the recent controversy in the scientific community related to the positive health effects of EPA and DHA on cardiovascular diseases (Chapter 4.2.5).

4.2 Fish consumption and cardiovascular disease

Fish consumption has been associated with protection against cardiovascular disease, both as a primary prevention (prevention of first time incidence of cardiovascular disease) and secondary prevention (prevention or intervention addressing recurrent disease). Mainly, the marine n-3 PUFA are nutrients identified as protective, although other complex interplay among a wide range of nutrients commonly found in fish may also play a role. On the other hand, mercury (methylmercury) from fish can increase the risk for cardiovascular diseases. Thus, consumption of fish with high mercury concentration (especially predatory fish and large/old freshwater fish) may increase the risk of developing cardiovascular diseases and/or neutralise the positive effect of marine n-3 fatty acids.

The FAO/WHO report (FAO/WHO, 2011) gave conclusions on possible risks and benefits of fish consumption on cardiovascular disease based on 19 prospective cohort studies and five clinical trials. They concluded that there was strong evidence that consumption of long-chain n-3 fatty acids from either fish or fish oil supplements lowers the risk of cardiovascular disease, especially death from coronary heart disease and sudden cardiac death. The dose-response relationship did not appear to be linear. A pooled analysis of 20 large studies in humans was found to support this non-linear effect for death from coronary disease, with a 36% risk reduction up to 250 mg EPA+DHA per day and then little additional lowering of risk at higher doses. Results were very similar when restricted to prospective cohort studies of seafood consumption in generally healthy (primary prevention) populations. Thus, overall benefits of fish or fish oil consumption for death from coronary heart disease appeared very similar in prospective cohort studies of fish consumption in generally healthy people (primary prevention) compared with controlled trials of fish oil in individuals with established heart disease (secondary prevention). Population groups included in these trials and cohorts which included studies in the USA, Europe, Asia and Australia varied, suggesting that coronary heart disease benefits are applicable across a wide range of countries and background diets. The Expert Consultation concluded that there is *convincing evidence* from extensive prospective cohort studies and randomised trials in humans of beneficial health outcomes from fish consumption for reduction of cardiac death, and there is also emerging, *possible or probable evidence* that fish consumption may reduce the risk of multiple other adverse health outcomes, including ischaemic stroke, non-fatal coronary heart disease events, congestive heart failure and atrial fibrillation. Furthermore, they concluded that the health benefits of fish are most likely due in large part to long-chain n-3 fatty acids, however, fish contain other nutrients that also may contribute. FAO/WHO also assessed the health risks associated with fish consumption, particularly relating to methylmercury and dioxins, based on previous JECFA evaluations (FAO/WHO, 2004; FAO/WHO, 2007) and focusing on new/additional information. They concluded that there is *an absence of probable or convincing evidence of risk* of coronary heart disease associated with methylmercury.

The Norwegian National Council for Nutrition came to the same conclusions as the FAO/WHO report on fish consumption (FAO/WHO, 2011) and n-3 fatty acids in fish and cardiovascular disease.

EFSA (2014b) restricted their cardiovascular endpoint to cardiac death. They based their conclusions on possible associations of fish consumption and cardiac death on six published meta-analyses of observational prospective cohort studies in adult populations without pre-existing coronary heart disease (CHD). The meta-analyses aimed at quantifying the relationship between seafood (or n-3 LCPUFA from seafood) consumption and risk of CHD mortality and were based on different combinations of the same 33 cohort studies. They also considered a draft version of a quantitative benefit analysis related to CHD mortality conducted by FDA in 2009. EFSA (2014b) concluded that the beneficial effects of seafood consumption on the risk of CHD mortality are observed at 1-2 servings of seafood per week and up to 3-4 servings per week compared to no seafood consumption. No benefit on CHD mortality might be expected at higher intakes (more than 4-5 servings per week). Such

benefits refer to seafood *per se* and include beneficial and adverse effects of nutrients and contaminants (e.g. methylmercury) contained in seafood (Chapter 4.2.4). It is furthermore concluded that health benefits of seafood consumption in reducing the risk of CHD mortality are probably owing to the content of n-3 LCPUFA in seafood. Due to the heterogeneity of the studies quantification of the benefit of seafood consumption on CHD mortality could not be done with sufficient certainty. Using n-3 LCPUFA intakes from seafood for the quantitative benefit analyses introduced an additional uncertainty in the benefit estimate.

In this updating of the 2006 VKM Report, five systematic reviews and meta-analyses, plus 19 cohort studies related to fish consumption and cardiovascular disease are included from the literature search (Appendix IV). The reviews and meta-analyses include partly overlapping sets of individual prospective cohort studies. In addition, brief summaries of some relevant studies on supplementary marine n-3 fatty acids and cardiovascular disease are also given.

In the following, brief descriptions of the systematic reviews and meta-analysis, and the relevant cohort studies of fish consumption and marine n-3 fatty acids from dietary fish consumption and cardiovascular disease published later than 2010, are briefly described. Cardiovascular diseases include several adverse health outcomes in addition to cardiac death.

4.2.1 Systematic reviews and meta-analysis, primary and secondary prevention

Zheng et al. (2012a) did an updated meta-analysis of **fish consumption and marine n-3 fatty acids contributed from dietary fish and coronary heart disease (CHD) mortality** to investigate the up-to-date pooling effects. They conducted a literature search in PubMed and ISI Web of Science for all relevant papers published in English-language journals up to September 2010, and they also reviewed secondary references if relevant. They included only prospective cohort studies which were providing risk estimates (relative risk (RR) or hazard ratio (HR) with the corresponding 95% confidence interval of CHD mortality rate for each category of fish consumption. In the meta-analysis the fish consumption was categorised into four groups based on the fish intake frequency. Seventeen cohorts with 315 812 participants and average follow-up period of 15.9 years were identified. Compared with the lowest fish intake (less than 1 serving per month or 1-3 servings per month), the pooled relative risk (RR) of fish intake on CHD mortality was 0.84 (95% CI: 0.75, 0.95) for low fish intake (1 serving per week), 0.79 (95% CI: 0.67, 0.92) for moderate fish intake (2-4 servings per week) (lower CHD mortality by 21%) and 0.83 (95% CI: 0.68, 1.01) for high fish intake (more than 5 servings per week). Furthermore, the dose-response analysis indicated that every 15 g/day increase of fish intake reduced the risk of CHD mortality by 6% (RR=0.94; 95% CI: 0.90, 0.98). The authors concluded that fish consumption of 1 serving per week or 2-4 servings per week has a significant protective effect on fatal CHD, the beneficial effect being stronger among those who had a moderate fish consumption (2-4 servings/week) than those who consumed low amounts of fish (1 serving per week). They also concluded that fish consumption of more than 5 servings per

week only marginally decreased CHD mortality, which could be attributed to the limited number of studies included in this category of fish consumption.

Djousse et al. (2012) conducted a meta-analysis to review current evidence on the association of **fish consumption and marine omega-3 (EPA and DHA) with the incidence of heart failure (HF)**. They identified relevant studies by searching MedLine, EmBase, Web of Science and CABI abstracts from 1966 up to August 31, 2011 without restrictions and by reviewing reference lists from retrieved articles. The meta-analysis was performed in accordance with the guidelines published by the Meta-analysis of observational studies in Epidemiology (MOOSE) group. Overall they included any paper that provided multivariate adjusted relative risk (RRs) and their corresponding 95% confidence intervals for HF, comparing categories of fish consumption, dietary intake or blood concentrations of EPA and DHA. If a study reported RR and 95% CI for men and women separately, and the effect of fish or EPA/DHA intake on the risk of HF was modified by sex, results by sex was treated as two separate studies in the meta-analysis. The quality of each study was assessed. Seven prospective studies (four in USA, three in Europe) with 176 441 participants in whom 5480 incident HF occurred, were retained. The average duration of follow-up was 13.33 years (range 7-16 years). Dietary assessment was obtained via food frequency questionnaires, and estimates of dietary EPA/DHA intake were derived from nutrient (four studies) or plasma phospholipid n-3 measurements (two studies). All reported relative measures of effect for HF in each study were adjusted for multiple covariates. Five prospective studies evaluated the associations between fish intake and incident HF. In the pooled analysis, a higher intake of fish (highest category in each study) was associated with a 15% (95% CI; 1-27%) lower risk of HF compared with the lowest category of fish intake (lowest category in each study). There was no evidence for heterogeneity among studies or publication bias. The authors concluded that the meta-analysis is consistent with a lower risk of heart failure with intake of marine n-3 fatty acids.

Li et al. (2013) conducted a meta-analysis of prospective cohort studies to determine whether **fish consumption could lower the incidence of heart failure (HF)**. They focused on dose-response relationship between fish intake and HF incidence. They conducted a systematic search of PubMed and EmBase from 1953 to June 2012 using keywords related to fish and HF and included studies with at least three categories of fish consumption reporting relative risk (RR) and corresponding 95% confidence interval (CI) for HF incidence. The primary outcome was incidence of HF and the definition of HF was accepted as reported in the individual study. Five prospective cohort studies (two conducted in USA and three in Europe) including 4750 HF events of 170231 participants and an average follow-up of 9.7 years were identified and selected. Two cohorts included only female participants, one included only male participants, and others included both males and females. Methods of dietary assessment of fish consumption were interviewer-administered questionnaire in one study, self-administered or WHO-administered questionnaire in other studies. Fish consumption was categorised into five standardised intervals. Compared with those who never ate fish or ate fish less than once a month, individuals who ate fish once a week exhibited a significantly lower risk of HF (RR: 0.91; 95% CI: 0.84, 0.99). The effect on

HF incidence seemed to increase with greater fish consumption. For individuals who consumed fish five or more times a week, the incidence of HF was decreased by 14% (RR= 0.86; 95% CI: 0.84, 0.99). There was no evidence of heterogeneity among the five studies. In the stratified analysis, gender and duration of follow-up did not modify the inverse association between fish consumption and incidence of HF. The pooled RRs did not statistically differ between studies and the sensitivity analysis indicated that diet assessment might not affect the outcome (for each category $p > 0.05$). The dose-response analysis (generalised least-square trend estimation) showed that for each 20 g/day increment in fish intake, the pooled RR was 0.94 (95% CI 0.90-0.97; p for trend = 0.001). This meta-analysis of prospective cohort studies indicates a substantial inverse association between fish consumption and HF incidence and suggests that fish intake once a week could reduce the HF. Furthermore, there is a dose-dependent inverse relationship between fish consumption and HF incidence.

Chowdhury et al. (2012) conducted a systematic review and meta-analysis on the association between **fish consumption, and marine n-3 fatty acids contributed from fish, and risk of cerebrovascular disease**, where 26 prospective cohort studies and 12 randomised controlled trials were included with aggregate data on 794 000 non-overlapping people from 15 countries and 34817 cerebrovascular outcomes. This review is an updated meta-analysis which further extend the findings of previous corresponding reviews (He, 2009; He et al., 2004; Larsson and Orsini, 2011) that higher fish consumption is moderately but significantly associated with a reduced risk of incident cerebrovascular disease (the relative risk, RR, of cerebrovascular disease for standardised categories of fish intake, typically adjusted for several conventional risk factors, for 2-4 versus 1 or less servings per week was 0.94 (95% CI 0.90-0.98) and for 5 or more versus 1 or less servings per week was 0.88 (0.81-0.96), based on 18 and 8 studies, respectively. In the dose-response meta- analysis (18 studies), an increment of two servings a week of any fish was associated with a 4% reduced risk of cerebrovascular disease (95% CI 1-7%). For all 21 studies, when comparing participants in the highest with the lowest category of fish intake, RR was 0.88 (0.84-0.93). In a subset of studies (62799 participants) the corresponding RR for white fish types was 1.03 (0.90-1.19) and for fatty fish types 0.84 (0.72-0.98). By contrast, dietary, circulating biomarkers in observational studies (14 prospective studies, involving 305119 participants and 5374 cerebrovascular outcomes recorded during an average follow-up ranging from four to 30 years), and supplements of longchain n-3 fatty acids in primary and secondary prevention trials (12 randomised controlled trials totalling 62040 participants during an average follow-up three years) were not significantly associated with risk of cerebrovascular disease, and similar results were obtained for ischaemic and haemorrhagic stroke events. The authors conclude that available data indicate moderate, inverse associations of fish consumption and long chain n-3 fatty acids with cerebrovascular risk. Long-chain n-3 fatty acids measured as circulating biomarkers in observational studies or supplements in primary and secondary prevention trials were not associated with cerebrovascular disease. Thus, the beneficial effects of fish intake on cerebrovascular risk might be mediated through a complex interplay among a wide range of nutrients commonly found in fish.

Xun et al. (2012) did a meta-analysis of prospective cohort studies through April 2012 to assess **association of fish consumption with risk of stroke and its subtypes accumulatively**. A systematic literature survey of MEDLINE and EMBASE was done. Additional information was retrieved through Google or a search of reference lists in relevant articles. A database was derived from 16 eligible studies (19 cohorts), including 402127 individuals (10568 incident cases) with a follow-up of an average of 12.8 years. The main outcome measure was the weighted hazards ratio (HR) and corresponding 95% confidence interval (CI) for incident stroke according to fish consumption using a random-effects model. Compared with those who never consumed fish or ate fish less than 1 per month, the pooled adjusted HRs of total stroke risk were 0.97 (95% CI 0.87-1.08), 0.86 (0.80-0.93), 0.91(0.85-0.98), and 0.87 (0.79-0.96) for those who consumed fish 1-3 per month, 1 per week and 5 or more per week, respectively ($P_{\text{linear trend}}=0.09$; $P_{\text{nonlinear trend}}=0.02$). Study location was a modifier, and an inverse association between fish intake and stroke incidence was only found in North America. The modest inverse association were more pronounced with ischemic stroke and were attenuated with haemorrhagic stroke. The authors conclude that there is accumulated evidence that suggests that fish intake may have a protective effect against the risk of stroke, particularly ischemic stroke.

4.2.2 Cohort studies, primary prevention

Levitan et al. (2009) conducted a population-based, prospective study of 39367 middle-aged and older Swedish men. Diet was measured using food frequency questionnaires. Men were followed for **heart failure (HF)** through Swedish inpatient and cause-of-death registers from 1 January 1998 to 31 December 2004. Proportional hazards models adjusted for age and other covariates were used to estimate hazard ratios (HR). Compared with no fish consumption, men who ate fatty fish once per week had an HR of 0.88 (95% CI 0.68–1.13). Hazard ratios for consumption two times per week and three times per week were 0.99 and 0.97, respectively. Hazard ratios across quintiles of marine omega-3 were 1, 0.94 (95% CI 0.74–1.20), 0.67 (95% CI 0.50–0.90), 0.89 (95% CI 0.68–1.16), 1.00 (95% CI 0.77–1.29). The authors concluded that in this population, moderate intake of fatty fish and marine omega-3 fatty acids was associated with lower rates of HF, though the association for fish intake was not statistically significant; higher intake was not associated with additional benefit.

Levitan et al. (2010) examined the association of fatty fish and marine omega-3 with heart failure (HF) in a population of middle-age and older women participating in the Swedish Mammography Cohort aged 48–83 years. Intake of fish and marine omega-3 was estimated from food frequency questionnaires. Women without history of **heart failure (HF), myocardial infarction, or diabetes** at baseline (n= 36234) were followed from January 1, 1998 until December 31, 2006 for HF hospitalisation or mortality through Swedish inpatient and cause-of-death registers; 651 women experienced HF events. Cox proportional hazards models accounting for age and other confounders were used to calculate incidence rate ratios (RR) and 95% confidence intervals (CI). Compared to women who did not eat fatty fish, RR were 0.86 (95% CI: 0.67, 1.10) for less than 1 serving per week, 0.80 (95% CI:

0.63, 1.01) for 1 serving per week, 0.70 (95% CI: 0.53, 0.94) for 2 servings per week, and 0.91 (95% CI: 0.59, 1.40) for 3 or more servings per week (p for trend=0.049). RR across quintiles of marine omega-3 fatty acids were 1 (reference), 0.85 (95% CI: 0.67, 1.07), 0.79 (95% CI: 0.61, 1.02), 0.83 (95% CI 0.65 - 1.06), and 0.75 (95% CI: 0.58, 0.96) (p for trend=0.04). The authors concluded that moderate consumption of fatty fish (one to two servings per week) and marine omega-3 fatty acids were associated with a lower rate of first HF hospitalisation or death in this population.

The population-based prospective study of women in Sweden examining the association between fish consumption and stroke incidence (Larsson et al., 2011), is included in the systematic review and meta-analysis of Chowdhury et al. (2012). Since this is a unique Scandinavian study on **stroke incidence** in women, a short study specific description follows. 34670 women (49-83 years of age) had a mean follow-up of 10.4 years, and 1680 strokes including 1310 cerebral infarctions, 233 haemorrhagic strokes and 137 unspecified strokes were diagnosed. They found that fish consumption was significantly inversely associated with risk of total stroke, but not cerebral infarction or haemorrhagic stroke. Comparison of women in the highest quintile of fish consumption (more than 3.0 servings of fish per week) had a 16% lower risk of stroke compared with women in the lowest quintile of fish consumption (less than 1.0 servings of fish per week); multivariate RR of total stroke was 0.84 (95% CI: 0.71-0.98, p for trend=0.049). Furthermore, consumption of lean fish, but not of other fish types, was inversely associated with risk of stroke. The multivariate RR of total stroke was 0.67 (95% CI: 0.49-0.93, p for trend=0.07 for 3 or more servings of lean fish per week with that of no fish consumption. The results suggest that the consumption of fish, especially lean fish, may reduce risk of stroke in women. The multivariate RR of total stroke was 0.67 (95% CI: 0.49-0.93, p for trend=0.07 for 3 or more servings of lean fish per week with that of no fish consumption.

Strom et al. (2011) examined the relationship between fish consumption and **the risk of cardiovascular disease** 12-17 years later in a Danish pregnancy cohort of 7429 relatively young and initially healthy women (the Aarhus Birth Cohort). In such a cohort a low number of cardiovascular events are expected. Therefore a mixed outcome was used, including cardiovascular diseases and hypertension (cardiovascular risk factor). Exposure information was derived from a questionnaire sent to the women in gestation week 16, and daily fish consumption was estimated. During the follow-up, 263 events of cardiovascular disease were identified at admission to hospitals. No association between cardiovascular disease and fish intake was found. The number of identified events of cardiovascular disease in the study may have been too low to detect a potential association between fish consumption and cardiovascular disease. The authors concluded that a protective effect of fish intake against cardiovascular disease could not be substantiated in a prospective cohort study of relatively young and initially healthy women who were followed up to 17 years through high quality registries.

Strom et al. (2012) assessed the association between intake of fish consumption and marine LCn3FAs and **the risk of cardiovascular disease** in a prospective cohort of young women

(mean age at baseline: 29.9 years [range: 15.7– 46.9]). Exposure information on 48627 women from the Danish National Birth Cohort was linked to the Danish National Patients Registry for information on events of hypertensive, cerebrovascular, and ischemic heart disease used to define a combined measure of cardiovascular diseases. Intake of fish and LCn3FAs was assessed by a food frequency questionnaire and telephone interviews. During follow-up (1996-2008; median: 8 years), 577 events of cardiovascular disease (328 hypertensive disease, 146 cerebrovascular disease, 103 ischemic heart disease) were found. Low LCn3FA intake was associated with an increased risk of cardiovascular disease (adjusted hazard ratio for women in lowest (3%, median 0.06 g/day) versus highest (median 0.73 g/day) LCn3FA intake group: 1.91 [95% CI 1.26–2.90]). Restricting the sample to women who had consistently reported similar frequencies of fish intake across three different dietary assessment occasions tended to strengthen the relationship (hazard ratio for lowest (0 g fish/day, median LCn3FA 0.10 g/day) versus highest intake (each week, median LCn3FA 0.60 g/day): 2.91 [95% CI 1.45–5.85]). Furthermore, the observed associations were consistent in supplementary analyses where LCn3FA intake was averaged across the three dietary assessment occasions, and the associations were persistent for all three of the individual outcomes. The authors concluded that the findings based on a large prospective cohort of relatively young and initially healthy women indicated that little or no intake of fish and LCn3FAs was associated with an increased risk of cardiovascular disease.

Five papers addressing fish consumption (lean or fatty fish) or intake of n-3 PUFA or adipose tissue content of n-3 PUFA and **cardiovascular disease** (two different adverse health outcomes) in healthy subjects in the Danish cohort (Diet, Cancer and Health), are individually summarised below.

Bjerregaard et al. (2010) studied the effect of fish consumption on **the risk of acute coronary syndrome (ACS)** in healthy subjects in Denmark. The study included 57053 men and women, 50-64 years in the Diet, Cancer and Health Cohort Study. The follow-up time was 7.6 years and a total of 1122 ACS were verified through nationwide medical databases. A detailed and validated food frequency questionnaire was used to estimate intake of lean and fatty fish. Among men, intake of fatty fish was associated with a lower risk of ACS, the hazard ratio was 0.67 (95% CI 0.53-0.85) when comparing the highest quintile of fish intake (more than 27 g/day) with the lowest quintile (0-6 g/day). The inverse association was observed for intake more than 6 g fatty fish per day, with no additional benefit for higher intakes. No associations were found for lean fish and ACS. Results were not consistent in women. The author concluded that a modest intake of fatty fish was associated with a lower risk of ACS in middle-aged men, while no consistent associations were found in women.

Joensen et al. (2010) assessed the hypothesis that dietary intake of marine n-3 PUFA is negatively associated with **the risk of acute coronary syndrome (ACS)** in healthy subjects. In the Danish Diet, Cancer and Health cohort study, 57 053 participants were enrolled. Dietary intake of total n-3 PUFA, including EPA, docosapentaenoic acid (DPA) and DHA, was assessed. During the mean follow-up period (7.6 years), 1150 cases of incident ACS diagnosis were identified in the Danish National Patient Registry or the Cause of Death

Registry. Diagnoses were verified through medical record review. In Cox proportional hazard models, adjustment for established risk factors for CHD was done. A borderline significant risk reduction of ACS was found in men only. Men in the four highest quintiles of n-3 PUFA intake (0.39 g or more n-3 PUFA per day) had approximately 15% lower incidence of ACS than men in the lowest quintile [the hazard ratios were 0.83 (95% CI 0.67, 1.03), 0.81 (95%CI: 0.65, 1.01), 0.90 (95%CI: 0.71, 1.13) and 0.81 (95%CI: 0.64, 1.04) for second, third, fourth and fifth (upper) quintile relative to lowest quintile of n-3 PUFA intake. There was no dose-response. Associations for EPA, DPA and DHA examined separately were all negative, but less consistent. No convincing associations were found among women. In conclusion, a borderline significant negative association was observed for intake of marine n-3 PUFA and ACS among healthy men.

Rix et al. (2013) examined the relationship between the content of total and individual marine omega-3 fatty acids in adipose tissue and the **development of atrial fibrillation (AF)** in a cohort study. A total of 57 053 Danish participants, 50-64 years of age were enrolled between December 1993 and May 1997 in the Diet, Cancer and Health Cohort Study. Eligible participants had to be born in Denmark, living in the urban areas of Copenhagen and Aarhus, and not be registered with a cancer diagnosis at the time of enrolment. For the present study, the study population consists of a randomly drawn sub-cohort of 3440 participants. The exposure was adipose tissue content of n-3 PUFA and the main outcome was incident AF during follow-up. An adipose tissue biopsy was taken from the buttocks of all participants at baseline. A total of 190 incidences of AF occurred during a median of 13.6 years of follow-up. Complete data were available for multivariate analysis in 3221 participants, including 179 cases of AF. The median adipose tissue content of total marine n-3 PUFA was 0.61% (5th/95th percentiles 0.35/1.08) in men and 0.65% (0.37/1.17) in women. The median intake of marine n-3 PUFA was 0.63 g/day as estimated by food frequency questionnaire at baseline. Incident AF was more common in men than in women. No statistically significant association between the adipose tissue content of n-3 PUFA and the risk of incident AF was found. However, the hazard ratio (HR) of AF indicated a protective trend (p=0.09). A similar trend towards a lower risk of AF was seen in the second (HR=0.87; 95% CI: 0.60, 1.24) and third tertile (HR=0.77; 95% CI: 0.53, 1.10) of marine n-3 PUFA compared with the lowest tertile. The authors concluded that there was no statistically significant association between the content of marine n-3 PUFA in adipose tissue and the development of AF; however data were suggestive of a protective trend.

In a follow up study in the same study population and using the full cohort (57 053 Danish participants aged 50-64 years and enrolled in the Diet, Cancer and Health Cohort Study between 1993 and 1997), (Rix et al., 2014) examined fish consumption marine n-3 PUFA assessed by the food frequency questionnaire in relation to **atrial fibrillation (AF)**. Complete data were available for multivariate analysis of 55 246 participants including 3284 cases of AF (2102 men and 1182 women). The median consumption of total marine n-3 PUFA was 0.63 g/day. Independent of whether the association between total marine n-3 PUFA and AF was modelled with marine n-3 PUFA as a continuous variable or according to quintiles, the results showed a U-shaped association with the lowest risk close to the median

intake and a higher risk at both lower and higher than median intake. The hazard ratio (HR) for the third versus the lowest quintile was 0.87 (95% CI 0.78–0.98). In secondary analyses, the model was also fitted for intake of total fish, lean fish, and fatty fish as well as separately for individual fatty acids EPA, DHA and DPA. For all exposures, the association was U-shaped, although less so for lean fish. The authors concluded that U-shaped association found in this study may explain some of the contradictory results from previous observational studies. They found no evidence of a beneficial dose-response effect at higher levels of consumption of marine n-3 PUFA and that only moderate consumption of marine n-3 PUFA may be preferable for primary prevention of AF.

Bjerregaard et al. (2010) studied the effect of fish consumption **on the risk of acute coronary syndrome (ACS)** in healthy subjects in Denmark. The study included 57 053 men and women, 50-64 years. The follow-up time was 7.6 years and a total of 1122 ACS were verified through nationwide medical databases. A detailed and validated food frequency questionnaire was used to estimate intake of lean and fatty fish. Among men, intake of fatty fish was associated with a lower risk of ACS, the hazard ratio was 0.67 (95% CI 0.53-0.85) when comparing the highest quintile of fish intake (more than 27 g/day) with the lowest quintile (0-6 g/day). The inverse association was observed for intake more than 6 g fatty fish per day, with no additional benefit for higher intakes. No associations were found for lean fish and ACS. Results were not consistent in women. The author concluded that a modest intake of fatty fish was associated with a lower risk of ACS in middle-aged men, while no consistent associations were found in women.

Amiano et al. (2014) examined whether dietary intakes of total omega-3 fatty acids (from plants and marine foods) and marine polyunsaturated fatty acids (PUFAs) (EPA, DHA) were associated with **the risk of coronary heart disease (CHD)** in men and women in the Spanish Cohort of the European Prospective Investigation into Cancer and nutrition (EPIC) project. A total of 41091 men and women aged 20-69 years were recruited 1992-1996. The mean follow-up was 10 years. A total of 609 participants (79% men) had a definite CHD event. A validated dietary questionnaire was used to estimate the intake of total omega-3 fatty acids. The fish intakes (g/day, mean (SD) were for men CHD 78.1 (48.4) and men cohort 77.1 (48.4), and for women CHD 56.6 (37.2) and women cohort 53.7 (34.7), while intakes of total omega-3 fatty acids (g/day, mean (SD) were for men CHD 1.7 (0.7) and men cohort 1.7 (0.7), and for women CHD 1.1 (0.5) and women cohort 1.2 (0.5) Only participants with definite incident CHD event classified as either definite (fatal or non-fatal acute myocardial infarction or unstable angina requiring revascularisation procedures) or possible (fatal or non-fatal myocardial infarction in those cases that did not meet all diagnostic criteria and fatal CHD with insufficient information) were considered as cases, Cox regression models were used to assess the association between the intake of total omega-3 fatty acids, EPA, DHA and CHD. Mean intake of total omega-3 fatty acids, EPA and DHA were similar in the cases and in the cohort. In the multivariate adjusted model, omega-3 fatty acids, EPA and DHA were not related to incident CHD in either men or women. The results did not change after exploring the consumption of fish by type, fatty or lean. The hazard ratios (HR) for omega-3 fatty acids were 1.23 in men (95% CI 0.94-15.9, p=0.20) and 0.77 in women (95%

CI 0.46-1.30, $p=0.36$). The authors concluded that in the Spanish EPIC cohort, with a relatively high intake of fish, no association between EPA, DHA and total omega-3 fatty acid intake and risk of CHD was found.

Association between consumption of fish (total, lean or fatty fish) and **venous thromboembolism (VTE)** was studied in a Danish follow-up study, Diet, Cancer and Health, including 27178 men and 29876 women recruited in 1993 and 1997, with no history of cancer (Severinsen et al., 2014). Information of fish intake and potential confounders were obtained from baseline questionnaires. The outcomes were incident VTE (all) and idiopathic VTE. During follow-up, ca. 10 years, 641 incident VTE events were verified. Cox proportional hazard models with age as time axis was used. No association between total fish intake (the 4 higher quintiles, 26 to more than 65 g total fish per day, compared to reference of 0-25 g total fish per day) and VTE was observed, but moderate intake (8 to 30 g per day) of fatty fish was associated with a statistically non-significant 20-40% lower risk of idiopathic VTE compared with low consumption (less than 8 g/day) of fatty fish. The authors concluded that intake of neither total nor fatty fish were statistically significantly associated with VTE events. However, intake of fatty fish may be associated with a reduction in risk of idiopathic VTE.

4.2.3 Cohort studies, secondary prevention

The following studies are included since they assess intervention with fatty (salmon) and lean fish, and/or Scandinavian patients.

Ramel et al. (2010) conducted a randomised, controlled dietary intervention trial (eight weeks) in 324 young overweight and obese (body mass index 27.5-32.5 kg/m²), normo- and hypertensive individuals from three European countries (Iceland, Spain and Ireland). The aim was to investigate whether salmon consumption three times a week improves **blood pressure**. The subjects were randomised to one of four energy restricted diets (-30% relative to estimated requirements): Salmon (150 g three times per week, resulting in a daily consumption of 2.1 g of n-3 LCPUFAs per day), cod (150 g three times per week, 0.3 g n-3 LCPUFAs), fish oil capsules (1.3 g n-3 LCPUFAs per day), or control (sunflower oil capsules, no seafood). Body weight, blood pressure (diastolic DBP and systolic SBP), and DHA (docosahexaenoic acid) in erythrocyte membrane were measured at baseline and endpoint. A significant weight loss and decreases in SBP and DBP after the intervention were found. The salmon and fish oil group had significantly lower DBP than the cod group, but not significantly lower than the control. The authors conclude that lower DHA content in erythrocyte's membrane at baseline, which might identify infrequent fish eaters, is associated with greater DBP reduction during an 8-week intervention providing seafood.

With the objective to study the relation between dietary intake of n-3 LC PUFAs or fish and **risk of future coronary events or mortality**, Manger et al. (2010) did an intervention sub study of participants in a the Western Norway B Vitamin Intervention Trial with a minimum follow-up of 57 months. Patients (2412), aged over 18 years diagnosed with well-

characterised coronary artery disease (CAD) (81% men) completed a food frequency questionnaire at baseline, from which daily intakes of DHA, DPA and EPA as well as fish were estimated on the basis of diet and intakes of food supplements. The main end point was a composite of coronary events, including coronary death, nonfatal acute myocardial infarction, and unstable angina pectoris. The mean intakes of n-3 LCPUFAs in quartiles 1-4 were 0.58 ± 0.29 , 0.83 ± 0.30 , 1.36 ± 0.44 , and 2.64 ± 1.18 g/day, respectively. No dose-response relation between quartiles of n-3 LCPUFAs (based on intake as the percentage of total energy) or fish and coronary events or separate end points was found. A slightly increased risk of coronary events at an intake of n-3 LCPUFAs less than ~ 0.30 g/day was seen. The authors concluded that secondary prevention with n-3 LCPUFAs or fish in this Norwegian population with established and well-treated CAD and with a relatively high intake of n-3 LCPUFAs had no significant effect on risks of coronary events and mortality. Only patients with very low intakes of n-3 LCPUFAs may reduce their risks of coronary events by increasing their intakes.

4.2.4 Fish consumption and exposure to contaminants and cardiovascular disease

The Expert Consultation (FAO/WHO, 2011) also assessed the health risks associated with fish consumption, particularly relating to methylmercury and dioxins, based on previous JECFA evaluations (FAO/WHO, 2004; FAO/WHO, 2007) and focusing on new/additional information. They concluded that there is an absence of probable or convincing evidence of risk of coronary heart disease associated with methylmercury.

The mercury opinion from EFSA in 2012 concluded that the observations related to the associations between mercury exposure and the endpoints myocardial infarction, heart rate variability and possibly blood pressure are of potential importance, but results were still not conclusive and were not used for risk assessment (EFSA, 2012a).

A summary of some more recent cohort studies and relevant Nordic studies relating to fish consumption and methylmercury, PCBs and/or dioxins are given below.

Virtanen et al. (2012) studied the association between serum n-3 LCPUFA (EPA, DPA and DHA), and hair mercury concentrations and **blood pressure** in middle aged and older men (848) and women (909), aged 53-73 years, from the Kuopio Ischaemic Heart Disease Risk Factor Study in Eastern Finland. Participants with ischaemic heart disease, stroke, diabetes, or hypertension treatment were excluded, leaving 396 men and 372 women. Log-transformed values were used to study associations. The participants were recruited between 1984-1989, and the follow-up period was 11 years. The mean serum concentrations were 1.63% (SD 0.91) for EPA, 0.77% (SD 0.16) for DPA, and 2.73% (SD 0.90) for DHA of all serum fatty acids. After multivariate adjustments, a higher serum EPA+DPA+DHA concentration was statistically significantly associated with a lower systolic blood pressure ($\beta = -4.41$; 95% CI: -6.95, -1.87) and pulse pressure ($\beta = -4.41$; 95% CI: -6.95, -1.87), but not with diastolic blood pressure ($\beta = -0.45$; 95% CI: -2.31, 1.52). Individual evaluation of

EPA, DPA and DHA gave similar associations. The mean hair mercury concentration was 1.42 µg/g (SD 1.54). Hair mercury was not associated with blood pressure and did not modify the association between PUFA and blood pressure. The authors conclude that in older men and women, higher serum n-3 PUFA levels, mainly reflecting fish intake in the study population, were associated with a modestly lower blood pressure. On the other hand, the environmental pollutant mercury present in fish was not associated with blood pressure.

Bergkvist et al. (2014) assessed the association between validated estimates of individual dietary PCB exposure, taking into account the fish consumption and the intake of long-chain omega-3 fatty acids, with the **risk of stroke and its subtypes** in a population-based prospective cohort study of middle-aged and elderly women (Swedish Mammography Cohort). The possible effects of factors (like parity, body mass) influencing the PCB body burden and date of birth (surrogate for prenatal exposure) were explored in stratified analyses. During 12 years of follow-up (397309 person-year), there were 2015 incident cases of total stroke (1532 ischemic strokes, 216 intracerebral haemorrhages, 94 subarachnoid haemorrhages, and 173 unspecified strokes). The mean energy-adjusted dietary exposure to PCBs was 192 ng/day (median 165 ng/day; 5th and 95th percentiles were 69 and 374 ng/day, respectively). Multivariable-adjusted relative risks (RR), controlled for known stroke risk factors and fish consumption, were 1.67 (95% CI 1.29-2.17) for total stroke, 1.61 (95% CI 1.19-2.17) for ischemic stroke, and 2.80 (95% CI 1.42-5.55) for haemorrhagic stroke for women in the highest quartile of dietary PCB exposure (median 288 ng/day) compared with women in the lowest quartile (median 101 ng/day). They concluded that in this population-based prospective cohort of middle-aged and elderly women, an exposure to PCBs from foods was associated with a statistically significant 67% increased risk of total stroke and almost 3-fold higher risk of haemorrhagic stroke when those in the highest exposure quartile were compared with those in the lowest. In contrast, the consumption of fatty fish and the intake of n-3 PUFA were associated with a decreased risk of total stroke. Further prospective studies are needed to clarify the concentrations of PCBs that may offset the beneficial effects of fish consumption.

In a case-control study in Sweden, in which data and samples were collected prospectively, Wennberg et al. (2011) assessed how fish consumption and erythrocyte concentrations of mercury (Ery-Hg) and selenium (Ery-Se) are related to the risk of **myocardial infarction** (MI) and whether n-3 fatty acids (EPA and DHA) in plasma phospholipids are protective. The study included 431 cases with a MI after data and sample collection, including 81 sudden cardiac death and 499 matched controls. Another 69 female cases with controls from a breast cancer screening registry were included in sex specific analyses. For the whole study group, the mean consumption and (range) of fish was 1.26 meals per week (0-8 meals per week). Median and (range) concentration of mercury in erythrocytes was 3.54 µg/l (0.01-87 µg/L) and the median relative level of EPA+DPA was 5.84% (2.78-14.5%). Odds ratios for the third compared with the first tertile were 0.65 (95% CI: 0.54-0.91) for Ery-Hg, 0.75 (95% CI: 0.53-1.06) for Ery-Se, and 0.78 (95% CI: 0.54-1.11) for plasma (P)-EPA+DHA. Ery-Hg and P-EPA+DHA were inter-correlated (Spearman's $R=0.34$): No association was seen for reported fish consumption. Multivariate modelling did not change these associations

significantly and sex-specific analyses showed no differences in risk associations. High concentrations of Ery-Se were associated with increased risk of sudden cardiac death. The authors concluded that the biomarker results indicate a protective effect of fish consumption. No harmful effect of mercury was indicated in this low-exposed population.

Wennberg et al. (2012) also assessed associations between exposure to both marine n-3 PUFAs and methylmercury and **myocardial infarction (MI)** using data from Finland and Sweden. Matched case-control sets were nested in population-based, prospective cohort studies including 361 and 211 men with MI from Sweden and Finland, respectively. MI risk was estimated in a logistic regression model with the amount of mercury in hair (hair-Hg) and concentrations of n-3 PUFAs (EPA+DHA) in serum as independent variables. The median hair-Hg was 0.57 µg/g and 1.32 µg/g in Swedish and Finnish controls respectively, whereas the percentage of PUFAs was 4.21% and 3.83%, respectively. In combined analysis, regression parameters showed that hair-Hg was associated with higher (p=0.005) and S-PUFAs with lower (p=0.011) MI risk. The model indicated that even a small change in fish consumption (i.e. increasing PUFA in serum by 1%) would prevent 7% of MIs, despite an increase in mercury exposure. However, at high hair-Hg, the modelled beneficial effect of PUFA on MI risk was counteracted by methylmercury. The authors concluded that exposure to mercury was associated with increased risk of MI, and higher S-PUFA concentrations were associated with decreased risk of MI. Thus, MI risk may be reduced by the consumption of fish high in S-PUFAs and low in methylmercury.

4.2.5 Supplementary n-3 fatty acids (EPA and DHA) and cardiovascular disease

There is convincing evidence that EPA and DHA prevent death from coronary heart diseases (Chapter 4.2). In 2011, VKM evaluated negative and positive health effects of n-3 fatty acids as constituents of food supplements and fortified foods (VKM, 2011b). The evaluation of positive health effects covered several health outcomes. For cardiovascular diseases it was concluded that the strongest evidence for possible beneficial effects of n-3 fatty acid supplementation in humans is provided by large randomised controlled trials involving more than 43000 study participants suffering from cardiovascular disease (secondary prevention). In patients given either 0.8 g EPA and DHA or 1.8 g of EPA as ethyl ester daily, the risk of cardiovascular events and mortality was reduced.

Primary prevention from EPA and DHA supplementation has been less studied. However, EFSA has based its recommendation for adults on scientific evidence indicating that fatty fish consumption (1-2 meals per week or dietary supplements containing EPA and DHA and equivalent to a range of 0.25 to 0.50 g of EPA and DHA daily) decrease the risk of mortality from coronary heart disease and sudden cardiac death (EFSA, 2010b).

During the last few years, several meta-analyses and systematic reviews including randomised controlled trials have assessed the beneficial effects of EPA and DHA on

cardiovascular risks. Thus, it was of special interest to assess if new evidence had emerged since 2011 related to the effects of supplemental EPA and DHA on cardiovascular diseases.

As described in Chapter 4.1.3, a literature search was conducted aiming to identify whether new scientific evidence would imply a change in the previously established beneficial effects of supplementary EPA and/or DHA in prevention of cardiovascular diseases. The majority of the studies conclude that EPA plus DHA lowers the risk of mortality from coronary heart disease. In addition, five meta-analyses not identified in the search were included in order to highlight and elaborate the recent controversy in the scientific community related to the positive health effects of EPA and DHA on cardiovascular diseases.

A systematic review on EPA and DHA and **cardiovascular disease** including 21 articles and 46737 subjects with high cardiovascular risk concluded that EPA and DHA reduced the risk of cardiovascular events and cardiac death (Delgado-Lista et al., 2012). In contrast, a systematic review and meta-analysis by Rizos and Elisaf (2013) reviewed 20 randomized control trials (RCTs) including 69680 patients, and concluded that EPA and DHA supplementation was not associated with a lower risk of all-cause mortality, cardiac death, sudden death, myocardial infarction and stroke. The opposite conclusions from these two meta-analyses despite a large overlap in the studies included reveal that there are differences in how the data are interpreted as well as differences in inclusion and exclusion criteria which can lead to different conclusions.

A recent meta-analysis based on 19 studies, including 24788 adult patients with impaired glucose metabolism, concluded that EPA and DHA had no protective effect on **cardiovascular mortality, major cardiovascular effects and all-cause mortality**, but reduced triglyceride level (Zheng et al., 2013a).

One systematic review compared low versus moderate intakes of EPA and DHA from supplements on **risk of coronary heart disease** in a total of 214426 healthy subjects aged 34 to 84 years old with a follow-up from four to 16 years (Musa-Veloso et al., 2011). They concluded that an intake of 250 mg EPA and DHA or more per day reduced the risk of sudden cardiac death.

A recent large double-blind, placebo controlled clinical trial including 12513 subjects with **multiple cardiovascular risk factors** received daily either 1g EPA and DHA or 1g olive oil as placebo with a median of five years follow-up (The risk and prevention study collaborative group). They concluded that a daily treatment with 1g EPA and DHA did not reduce cardiovascular mortality and morbidity. This trial has received some critical comments particularly since they changed the primary end point during the trial due to a low incidence of cardiovascular events and for using olive oil as placebo because olive oil may reduce primary cardiovascular events (Estruch et al., 2013).

Based on the above mentioned studies, e.g. inclusion and exclusion criteria, doses of EPA and DHA, composition of placebo, type of subjects i.e. healthy, healthy but at high risk of cardiovascular disease or patients, and subjects with or without impaired glucose control all

seem to affect the health outcome from supplementary EPA and DHA. In addition, the background diets will also affect the baseline levels of EPA and DHA. In a review by Ramsden et al. (2010) they show that the relative amount of n-6 fatty acids to n-3 and amounts of ALA versus EPA and DHA both affects the end points and thereby the conclusions, i.e. that a high intake of n-6 fatty acids may actually increase the risks of CHD and death. The supplemental ALA given to individuals on a Western diet does not have the same beneficial effects as EPA and DHA on the vascular system or on the biomarkers of disease risk e.g. serum triacylglycerols.

Despite some conflicting findings i.e. no beneficial versus beneficial effect, in reviews and meta-analyses regarding the effects of supplementary EPA and DHA on cardiovascular diseases, new scientific evidence does not imply a change in the previously established beneficial effects of supplementary EPA and/or DHA in prevention of cardiovascular death.

4.3 Fish consumption and outcomes related to the central nervous system; main focus on neurodevelopment

In 2006, VKM summarised that it appeared that marine n-3 fatty acids have a positive impact on length of pregnancy and foetal development. Although studies of fish consumption have not shown that n-3 LCPUFA have a positive effect on the development of the central nervous system (CNS) of foetuses and newborn babies, this has been shown to be the case in other studies involving n-3 LCPUFA supplementation. Methylmercury in fish may damage the brain development of the foetus and infant. In 2006, VKM did not assess other CNS related outcome than neurodevelopmental ones.

A number of fatty acids, particularly the marine n-3 fatty acid DHA, are essential for the development of the central nervous system of humans, and there is a growth spurt during the last trimester of pregnancy and during the first months *post partum* as well as important development up to two years of age. Thus, neurodevelopment of foetus and children is a most sensitive health outcome.

4.3.1 Neurodevelopmental outcomes

The national and international health authorities FAO/WHO, the Norwegian National Council for Nutrition and recently EFSA have all assessed possible effects (beneficial and adverse) of seafood consumption before and/or during pregnancy on functional outcomes of children`s neurodevelopment in 2011, 2011 and 2014, respectively.

The EFSA Opinion on mercury in 2012 based the TWI on neurodevelopment in children (EFSA, 2012a). Recently, EFSA addressed benefits of seafood consumption in relation to functional outcome of children`s neurodevelopment (EFSA, 2014b). Furthermore, the US Food and Drug Administration also recently published an extensive quantitative assessment of the net effects on foetal neurodevelopment of eating commercial fish during pregnancy (FDA, 2014).

The conclusions from the abovementioned assessments/reviews of data on fish consumption and neurodevelopmental outcomes all form the basis for the present VKM assessment of epidemiological studies addressing risks and benefits of fish consumption of women of childbearing age and optimal neurodevelopment of their offspring, and their conclusions are briefly summarised below:

FAO/WHO (2011) concluded that multiple observational studies have demonstrated independent beneficial associations with fish consumption during pregnancy, DHA levels in maternal blood during pregnancy or in cord blood during delivery with more optimal neurodevelopmental outcomes, including better behavioural attention scores, visual recognition, memory, and language comprehension in infancy and childhood, in the offspring (FAO/WHO, 2011). Thus, there is *convincing evidence* (Table 4.1) that fish consumption by women reduces the risk of suboptimal neurodevelopment by their offspring. Randomised controlled trials with DHA supplementation during nursing support this finding. The FAO/WHO report concludes that together, maternal consumption of n-3 LCPUFAs during pregnancy and nursing improves early brain development in children. Fish, however, contain other nutrients that may also contribute to the health benefits of fish.

Furthermore, FAO/WHO concluded that there is *convincing evidence* (Table 4.1) of adverse neurological/neurodevelopmental outcomes in infants and young children associated with methylmercury exposure during foetal development due to maternal fish consumption during pregnancy. FAO/WHO also concluded that there is *insufficient evidence* (Table 4.1) for adverse health effects (e.g. endocrine disruption, immunological and neurodevelopmental effects) associated with exposures to dioxins from fish consumption. Among infants and young children the available data are insufficient to derive a quantitative risk-benefit assessment.

The conclusions of FAO/WHO are in particular based on the two largest longitudinal studies of neurobehavioral development in children carried out in the Seychelles and the Faroe Islands in populations consuming fish/seafood. It should be noted that the diet in the Faroe Islands includes fish and episodic consumption of marine mammals, in particular pilot whales, which constitute the major dietary source to methylmercury. Beneficial effects of fish consumption might confound the neurotoxic associations in the Faroese studies, causing underestimation of the effects of methylmercury. The Seychelles Child Development Study was designed to study the developmental effects of prenatal exposure to methylmercury in a fish-eating population. No significant neurobehavioural deficits in children regardless of their age were found.

The Norwegian National Council for Nutrition (2011) came to the same conclusions as FAO/WHO (2011) on fish consumption and n-3 fatty acids in fish and neurodevelopmental outcomes.

EFSA (2012a) assessed risk from mercury exposure, and did not assess the nutritional benefits linked to certain foods. Neurodevelopmental endpoints are the critical end point for methylmercury exposure and unborn children constitute the most vulnerable group (Chapter

2.3.1). For methylmercury, new developments in epidemiological studies from the Seychelles Child Developmental Study Nutrition Cohort have indicated that n-3 LCPUFAs in fish may counteract negative effects from methylmercury exposure. Together with the information that beneficial nutrients in fish may have confounded previous adverse outcomes in child cohort studies from the Faroe Islands, the Panel established a TWI for methylmercury of 1.3 µg/kg bw, expressed as mercury. EFSA (2012a) included new follow-up data from the Faroe Islands Cohort of the children at the age of 14 years, which indicated that the association between prenatal exposure and neurological auditory function was still present at 14 years. Furthermore, reassessment of the data at the follow-up at seven years of age indicated that beneficial effects of fish consumption together with imprecision in the measurement of fish consumption and the determination of mercury in hair might underestimate the effects of methylmercury. EFSA (2012a) also referred to reassessments of the 4.5 years results and the 10.5 and 17 years follow up studies from the Main Cohort in the Seychelles Child Development Study, which indicated no consistent association between prenatal mercury exposure and neurodevelopmental endpoints. New results from the smaller Nutrition Cohort in the Seychelles Child Development Study indicated an association between prenatal mercury exposure and decreased scores on neurodevelopmental indices at nine and 30 months after adjustment for prenatal blood maternal n-3 LCPUFAs. No statistically significant associations were found at the five years follow up between prenatal mercury exposure and developmental endpoints. A positive association between maternal prenatal n-3 LCPUFAs and preschool language was reported from the five years follow up study.

In 2014, both taking into consideration the above mentioned FAO/WHO Report (FAO/WHO, 2011) and the EFSA report (EFSA, 2012a), as well as the US Food and Drug Administration report from 2014 (FDA, 2014), the EFSA Panel on Dietetic Products, Nutrition and Allergies has recently evaluated the beneficial effects of seafood and marine n-3 PUFA during pregnancy on functional outcomes of children's neurodevelopment (EFSA, 2014b). Data from observational studies on seafood consumption during pregnancy, intakes of n-3 LCPUFA from seafood during pregnancy, observational studies on biomarkers of maternal n-3 LCPUFA during pregnancy or at delivery, and also intervention studies with n-3 LCPUFA supplementation during pregnancy have been reviewed. They concluded that there are significant positive associations between fish/seafood consumption during pregnancy and children's neurodevelopment. These observations were observed for fish/seafood intakes of about 1-2 servings per week and up to 3-4 servings per week compared to no seafood intakes, and refer to fish/seafood per se, including nutrients (e.g. DHA, iodine) and contaminants (such as methylmercury) contained in fish/seafood. There appear to be no additional benefit with higher fish consumption. The observed positive health effects of fish consumption during pregnancy may depend on maternal status of nutrients (e.g. DHA, iodine) that have an important role in neurodevelopment of the foetus, and on the independent role of fish/seafood to provide these nutrients. That no evidence is found for an effect of DHA supplementation during pregnancy on children's neuro-developmental outcomes support this. The data from the various studies are not easily comparable because of differences in neurodevelopmental tests used, testing at different ages, and uncertainties and differences in the estimation of fish/seafood consumption. The heterogeneity of the

studies thus hampers quantitative risk-benefit analyses of fish consumption and risk of a neurodevelopmental outcome.

In May 2014, US Food and Drug Administration (FDA) published a quantitative assessment of the net effects on foetal neurodevelopment of eating commercial fish during pregnancy (FDA, 2014). This assessment was a modified and expanded version of the original assessment first issued by the FDA in 2009. The modelling in the recent assessment provides estimates for the net effects of eating commercial fish on three neurodevelopmental endpoints: IQ at nine years of age (the primary modelling), early age verbal development through about 18 months of age (secondary modelling), and later age verbal development through nine years of age (included for purposes of comparison). The assessment estimates that for each of the endpoints modelled, consumption of commercial fish during pregnancy is net beneficial for most children in the USA. On a population basis, average neurodevelopment in USA is estimated to benefit by nearly 0.7 of an IQ point (95% CI of 0.39-1.37 IQ points) from maternal consumption of commercial fish. For comparison purposes, the average population-level benefit for early age verbal development is equivalent in size to 1.02 of an IQ point (95% CI of 0.44-2.01 IQ size equivalence). For a sensitive endpoint as estimated by tests of later age verbal development, the average population level benefit from fish consumption is estimated to be 1.41 verbal IQ points (0.91, 2.00). The assessment also estimates that depending on the fish types and amounts of fish, fish consumption may give a mean maximum improvement of about three IQ points. Fish lower in methylmercury generally give larger benefits than fish higher in methylmercury. The size of the adverse net effects are estimated to range from -0.01 of an IQ point (95% CI of -0.13-0.00) to -0.05 of an IQ point (95% CI of -0.56, 0.00). The net effects modelling for both early and later age verbal development do not estimate that adverse net effects are likely for these endpoints. However, the confidence intervals do estimate small possibilities of faint adverse net effects through at least 10% of children for early age verbal development and 25% of children for later age verbal development. These results are at least suggestive of adverse effects when fish consumption is not sufficient to outweigh the adverse effects of methylmercury. The assessment also modelled 47 individual commercial fish species and market types. The results were consistent with the population-level results. Almost all species and market types were estimated to become net beneficial at relatively low levels of consumption. The beneficial net effect increases with consumption up to about 12 ounces per week (approximately 340 g) until a maximum possible benefit around three IQ is reached.

The literature search done (Chapter 4.1) did not reveal relevant studies on fish consumption and neurodevelopment. The only relevant study on fish consumption and neurodevelopment found addressed negative confounding by n-3 LCPUFA on the association between methylmercury exposure and neurodevelopment in the Faroe Islands and is summarized below.

Choi et al. (2014) assessed the potential impact of negative confounding by DHA and EPA on the methylmercury effects on children's neurobehavioural performance by examining 176

Faroese children, in whom prenatal methylmercury exposure was assessed from mercury concentrations in cord blood (geometric mean 21.4 ug/L) and maternal hair (geometric mean 4.10 ug/g). The relative concentrations of fatty acids were determined in cord serum phospholipids (sum DHA and EPA ug/L mean (SD) 9.57 (1.71), and neuropsychological performance in verbal, motor, attention, spatial, and memory functions was assessed at seven years of age. Multiple regression and structural equation models (SEMs) were carried out to determine the confounder-adjusted associations with methylmercury exposure. A short delay recall (% change) in the California Verbal Learning test was associated with a doubling of cord blood methylmercury (-18.9, 95% CI: -36.3, -1.51). The associations being stronger after the inclusion of fatty acid concentrations in the analysis (-22.0, 95% CI: -39.4, -4.62). In structural equation models, poorer memory function was associated with a doubling of prenatal exposure to methylmercury after the inclusion of fatty acid concentrations in the analysis (-1.94, 95% CI: -3.39, -0.49). The authors concluded that association between prenatal exposure to methylmercury was associated with deficits in school age in domains known to be sensitive to this neurotoxicant, with associations being strengthened after fatty acid adjustment. Thus, beneficial effects of fish consumption may confound the neurotoxic associations with neurobehavioural performance.

In the following, systematic reviews and meta-analyses, and some relevant cohort studies of fish consumption and marine n-3 fatty acids from dietary fish consumption and various CNS outcomes published later than 2009, are briefly described.

4.3.2 Cognition

In a randomised control trial in schoolchildren (seven to nine years) from the northern Cape Province of South-Africa, Dalton et al. (2009) investigated the effect of an experimental fish-flour bread spread rich in n-3 long-chain fatty acids, on **cognition**. The children were randomly assigned to an experimental (n=91) and control group (n=92), receiving either the fish flour spread or a placebo spread for 6 months in a single-blind study. Short dietary questionnaire revealed no intake of fatty fish and a very low intake of lean fish in this community. Plasma and red blood cell phospholipid fatty acid composition and cognition (*Hopkins Verbal Learning Test Recognition*, *Discrimination Index* and *Spelling test*) were measured at baseline and post-intervention. After the intervention EPA and DHA levels were significantly higher in the experimental group compared to the control group (p<0.0001). Significant effects on cognition outcomes were also observed for the *Hopkins Verbal Learning Test Recognition* (estimated effect size: 0.80; 95% CI: 0.15, 1.45) and *Discrimination Index* (estimated effect size: 1.10; 95% CI: 0.30, 1.91), as well as *the Spelling test* (estimated effect size: 2.81; 95% CI: 0.59, 5.02 by both per protocol and intention to treat analyses. A tendency to improvement was observed for the *Reading test*. The authors suggest that children when supplemented with a fish-flour spread rich in n-3 long-chain fatty acids have improved verbal learning and memory.

In a longitudinal cohort study, Aberg et al. (2009) evaluated fish consumption related to later **cognitive performance** in healthy young male adolescents (15-year-olds). In 2000, all 15-

year-olds in the western region of Sweden were requested to complete an extensive questionnaire with items on diseases, fish consumption and socioeconomic status. Questionnaire data from the male responders (n=4792, response rate 52%) were linked with records on subsequent intelligence test performance at age 18 from the Swedish Military Conscription Register (n=3972). Multivariate linear models were used to estimate associations between fish intake and cognitive performance, adjusting for potential confounders. They observed a positive association between the number of times having fish meals per week at age 15 and cognitive performance measured three years later. Fish consumption of more than once per week compared to less than once per week was associated with higher stanine scores (method of scaling test scores on a nine-point standard scale with a mean of five and a standard deviation of two) in combined intelligence (0.58 units; 95% confidence interval 0.39, 0.76), in verbal performance (0.45; 0.27, 0.63) and in visuospatial performance (0.50; 0.31, 0.69). The association between fish consumption and the three intelligence scores was the same in lowly and highly educated groups. This indicates that education did not influence the association between the frequency of fish meals consumed and cognitive performance. The authors concluded that frequent fish intake at age 15 was associated with significantly higher cognitive performance three years later.

Kim et al. (2010) studied the associations between fish intake and **academic achievement** as cognitive parameters among Swedish school children (n= 18158), aged 15 years. In 2010 a questionnaire including respiratory items, socioeconomic conditions and dietary information was mailed to the school children. One year later, the total school grades for each individual who had completed the questionnaire (n=10837), and who included their full identification number were obtained from national registers (n=9448; 49.5% boys, 11.7% of foreign descent). Multiple linear regression models were used and adjustments for confounders applied. When grades of subjects in the highest category of fish consumption were compared with grades of subjects with fish consumption of less than once a week (reference group) the total mean score was 225.5 vs. 196.6 (p<0.001). Compared with the reference group grades were higher in subjects with fish consumption once a week (increment in estimate 14.5; 95% CI: 11.8, 17.1), and even higher in subjects with fish consumption more than once a week (increment in estimate 19.9; 95% CI: 16.5, 23.3). There were strong association between parents' education and school children's grades. In the model stratified for parents education, there were still higher grades among school children with frequent fish intake in all educational strata (p>0.01). The authors concluded that frequent fish intake among school children may provide benefits of academic achievement.

4.3.3 Cognitive decline (dementia, Alzheimer's disease)

Fotuhi et al. (2009) performed a systematic review of the literature (MEDLINE and Cochrane database from January 1980 to September 2008) to determine the strength of evidence for the use of fish consumption and n-3 fatty acids in relation to **cognitive impairment and dementia, including Alzheimer's disease (AD)**. They identified 11 observational studies and four small randomised clinical trials on the association between n-3 fatty acids (either in the diet or in the form of supplements) and cognition, dementia, mild cognitive impairment

or AD. Three observational studies (total n= 4174, age 63-89 years) that used cognitive decline as outcome reported significant benefits, while only four out of eight observational studies (total n=18720, age 55-88 years) that used incidence of AD or dementia as outcome reported positive findings. None of the clinical trials (total n=535) provided convincing evidence for the use of n-3 fatty acids in the prevention of or treatment of any form of dementia. The authors conclude that the systematic review of observational studies suggests that long-chain n-3 fatty acids provide a modest benefit with regard to slowing cognitive decline among elderly individuals without dementia. By contrast, clinical trials have failed to detect any beneficial role of the use of EPA, DHA or other forms of n-3 fatty acids for secondary prevention or treatment of AD.

Cederholm and Palmblad (2010) have reviewed recent data (13 recent observational studies, seven using biochemical indicators and six using dietary recalls for assessment of n-3 levels, three randomised intervention studies with duration up to 6 months, and several experimental studies) on the potential role of n-3 fatty acids found in oily fish, especially DHA, to prevent and treat **cognitive decline and Alzheimer's disease**. Observational studies provide conflicting results, however the majority of results indicate beneficial effects on cognition both when assessed as a continuous variable or as incident dementia, mainly Alzheimer's disease. Experimental studies suggest that n-3 fatty acids play a role in primary prevention of cognitive decline by improving blood flow, decreasing inflammation and/or reducing amyloid- β pathology. No positive overall effects were reported from the intervention studies. The authors conclude that no firm conclusions can be drawn.

Huang (2010) did a critical review and evaluation of the literature regarding omega-3 fatty acids, **cognitive decline, and Alzheimer's disease (AD)**. He used Ovid Medline databases and restricted his search to include only human studies written in English. Furthermore, for each original and review paper found, references were searched for additional relevant papers. Nine studies that examined cross sectional relationships between either plasma, erythrocytes, dietary fatty acids, or fish and dementia, AD, or cognitive functioning, 27 relevant prospective studies and eight relevant clinical trials were identified. While cross sectional studies imply that n-3 fatty acids might be protective against cognitive decline and AD (five of six studies found a relationship between n-3 fatty acids measured in blood or plasma and cognitive decline, with better outcomes associated with higher total n-3 fatty acids or DHA, all three studies that examined fish oil or DHA intake found it to be associated with better scores on cognitive tests, and all three studies that examined fish intake showed a positive association between fish consumption and cognitive scores), it is also likely that one's diet could change as a result of cognitive impairment. An additional study examining 14960 residents across seven countries found that the relationship between fish consumption and prevalence of dementia differed between countries suggesting that fish is protective under a particular set of circumstances, but that it depends on a variety of factors not yet accounted for. With longitudinal studies, findings with fish intake have been more consistently seen as protective. This may be because fish intake is easier to measure than n-3 fatty acids from multiple sources, or there may be important nutrients in fish that are fundamental to optimal absorption and use of DHA and/or EPA. Ten of eleven studies

examining fish intake, found significant or non-significant protective effect associated with dementia, AD, or cognitive decline; in seven studies a minimum of one to two fish meals per week were required to show an effect; in five studies there was a dose-responsive decline in risk with increasing consumption. No definite conclusion can be made from the clinical trials where supplementation was done with one or a mixture of n-3 fatty acids. The variability in outcomes between human studies which are confounded by methodological differences, make it difficult for conclusions to be drawn. The author concluded that even though there is strong evidence from animal studies that n-3 fatty acids and particularly DHA is protective against cognitive decline, AD, and its underlying neuropathology via a variety of different mechanisms of action, results across the literature in humans (from epidemiological studies, studies of post-mortem n-3 fatty acids in the brain, and clinical trials) are inconsistent and thus difficult to interpret.

Danthiir et al. (2014) examined associations between multiple domains of **cognition and erythrocyte membrane n-3 PUFA proportions** and historical and contemporary fish intake in 390 normal older adults, analysing baseline data from the Older People, omega-3, and Cognitive Health Trials in Australia. They found no evidence of a beneficial effect of increased long-chain n-3 fatty acid concentrations or fish intake on baseline cognitive performance in cognitively normal older adults.

4.3.4 Depressive episodes and psychological distress

Suominen-Taipale et al. (2010) did a cross-sectional analysis to evaluate whether higher fish consumption and n-3 fatty acids intake are associated with lower 12-month prevalence of **depressive episodes** in the Finnish adult population and in a Finnish population with high fish consumption. Two cross-sectional data sets gathered in Finland were used; the nationwide HEALTH 2000 Survey (n=5492) and the Fisherman Study on Finnish professional fishermen and their family members (n= 1265). Data were based on questionnaires, interviews, health examinations, and blood samples. The Munich version of the Composite International Diagnostic Interview (M-CIDI) and a self-report of two CIDI probe questions were used to assess depressive episodes. Fish consumption was obtained from a food frequency questionnaire (g/day) and independent frequency questions (times per month). Dietary intake (g/day) and serum concentrations (% from fatty acids) of PUFAs were determined. Fish consumption was associated with decreased prevalence of depressive episodes in men. In the women, no consistent associations between fish consumption and age-adjusted prevalence of depressive episodes were found. The prevalence of depressive episodes decreased from 9% to 5% across the quartiles of fish consumption (g/day) in men of the Health 2000 Survey (p for linear trend =0.01), from 17% to 3% across the quartiles of fish consumption (times per month) in men of the fishermen Study (p for linear trend =0.05). The association was modified by lifestyle. The authors concluded that for men but not women, the results give some support to the hypothesis that high fish consumption protects against depression. However, since there were no associations between n-3 PUFAs and the occurrence of depressive episodes, they suggest that the beneficial effect in men

may be associated with other nutritional compounds in fish, and complex associations between depression and lifestyle may also play a role.

Suominen-Taipale et al. (2010) utilised three distinct cross-sectional data sets; the Health 2000 survey (carried out in 2000/2001, n=8208, participants aged 30 years or more) representing the general population of Finland; the Fishermen Study (Finnish fishermen and their family members, n= 1282) representing a population with high fish consumption, and the Finntwin16 Study (young adults, n= 4986) representing young adults, to assess whether high fish consumption and n-3 PUFA intake was associated with reduced self-reported **psychological distress**, as measured by the General Health Questionnaire (GHQ). Data were based on self-administered questionnaires, interviews, health examinations and blood samples. Psychological distress was measured using the 12-item and 21-item GHQs. Fish consumption was obtained from a food frequency questionnaire (g/day) and independent frequency questions (times per month). Dietary intake (g/day) and serum concentrations (% from fatty acids) of PUFAs were determined. Relations were analysed by regression analysis. No associations were found between fish consumption and n-3 PUFA dietary intake and psychological distress regardless of measure in any of the data sets. The authors concluded that the results do not support the hypothesis that fish consumption or n-3 PUFA intake are beneficial for psychological distress in the general population or in a population with high fish consumption.

4.4 Fish consumption and cancer

Based on experimental animal data it is biologically plausible that n3-PUFA in fish protect against various types of cancer, however, the data from epidemiological studies are not clear. In 2006 VKM summarised data on breast cancer, colorectal cancer, prostate cancer and thyroid cancer and concluded that fish consumption shows no reliable correlation with the development of cancer.

(WCRF, 2007) concluded that there is limited – suggestive evidence that fish and also food containing vitamin D protect against colorectal cancer. They also concluded that there is probable increased risk of cancer in nasopharynx with consumption of Cantonese-style salted fish. The results from WCRF was referred to by the Norwegian Directorate of Health, they regarded Cantonese-style salted fish as not relevant for Norway (Norwegian National Council for Nutrition, 2011).

From the literature search, 20 papers addressing fish consumption and cancer were selected for review in full-text. Of these, 14 reviews and meta-analyses have been briefly summarised below. In addition, a meta-study on colorectal cancer was published in 2007 (Geelen et al., 2007). This study, along with a Norwegian study published in 2007 (Engeset et al., 2007), was included in the WCRF report in 2007.

4.4.1 Breast cancer

Zheng and Li (2013) reported a meta-analysis of data from 21 independent prospective cohort studies. Their search in PubMed and Embase covered the time up to December 2012. The eligibility criteria were prospective studies reporting RR and 95% CI according to fish intake, n-3 PUFA intake, or tissue biomarkers, resulting in 20905 cases of breast cancer and in total 883585 participants from the United States, Europe and Asia. Quality assessment was conducted according to Newcastle-Ottawa criteria for non-randomised studies.

The associations between **breast cancer** risk and fish consumption and breast cancer risk and consumption of marine n-3 PUFA were reported separately. Combined results from 11 studies from 11 independent cohorts, comparing lowest and highest n-tile of fish consumption in each study (13323 breast cancer events, 687770 participants) on association between fish consumption and breast cancer risk, did not show association (RR=1.03; 95% CI: 0.93, 1.14). The study heterogeneity was reported as moderate, but no publication bias was observed. No dose – response was observed by 15 g/day increment of fish consumption.

The analysis of marine n-3 PUFA consumption and risk of breast cancer involved 17 papers on 16 independent cohorts (16178 breast cancer events, 527392 participants). Marine n-3 PUFA intake was inversely associated with risk (RR=0.86; 95% CI: 0.78, 0.94). Dose-response analysis indicated 5% reduction in risk with 0.1g/day or 0.1% energy increment of daily marine n-3 PUFA intake from fish. No study heterogeneity was observed. The association was present in both western and Asian countries, but was most prominent in Asian countries, where fish consumption was higher than in Europe and the USA.

The authors concluded that their results provide solid and robust evidence that increased intake of marine n-3 PUFA from fish resulted in reduced risk of breast cancer, and that the protective effects of fish warrants further investigation in prospective studies.

4.4.2 Prostate cancer

Szymanski et al. (2010) conducted a review and meta-analysis of cohort and case-control studies on fish intake and **prostate cancer** (incidence and prostate cancer-specific mortality, including cancer grade and stage). Their literature search covered Medline and Embase up to May 2009. The results showed no significant association between prostate cancer incidence and fish consumption when comparing lowest and highest quantile of fish consumption. The conclusion was based on 12 case-control studies (5777 cases and 9805 controls, odds ratio (OR)=0.85 (95% CI 0.72, 1.00) and 12 cohort studies (445820 participants, 13 924 prostate cancers, RR=1.01 (95% CI 0.90, 1.14). There was significant heterogeneity between the case-control studies, but not between the cohort studies after exclusion of one paper. There was no indication of publication bias. Based on results from four cohort studies they found a significant association between fish consumption and

reduction in prostate cancer specific mortality (49661 men, 740 fatal prostate cancers, RR=0.37 (95% CI 0.18, 0.74).

The authors concluded that their analyses of observational studies provided little evidence of a protective association of fish consumption with prostate cancer incidence, and that additional studies on aggressive and fatal disease are needed.

4.4.3 Gastrointestinal cancer

In a systematic review and meta-analysis, Han et al. (2013) addressed fish consumption and risk of different types of **cancers in the oesophagus**. Based on 21 case-control and three cohort studies included (6677 cases) identified by search in Medline or Embase up to May 2012, the RR for squamous cell carcinoma was 0.81 (95% CI: 0.66, 0.99) with significant study heterogeneity, and for adenocarcinoma 0.86 (95% CI: 0.61, 1.22). The authors concluded that fish consumption is not appreciably related to risk of squamous cell carcinoma or adenocarcinoma in the oesophagus.

Salehi et al. (2013) conducted a systematic review and dose-response meta-analysis of associations between **oesophageal cancer** risk and consumption of meat and fish in published studies (1990-2011 in Medline, Embase and Web of Knowledge) using MOOSE guidelines (5689 cases). Data from the 17 studies reviewed suggest there is a modest inverse association between fish consumption and EC risk (RR for highest vs lowest intake was 0.80; 95% CI: 0.64, 1.00), but there was considerable heterogeneity among the studies. The authors concluded that the results suggest that low levels of red and processed meat consumption and higher levels of fish intake might reduce oesophagus cancer risk.

Wu et al. (2011) gave a systematic review and meta-analysis of association between fish consumption and **gastric cancer** risk covered the available literature in PubMed up to January 2009, and selected 15 case-control studies and two prospective cohorts. No statistically significant association was seen (5323 cases, more than 130000 non-cases, RR=0.87; 95% CI: 0.71, 1.07).

As mentioned above, the World Cancer Research Fund (WCRF) concluded in 2007 that there is *limited – suggestive evidence* (Table 4-1) that fish and also food containing vitamin D protect against **colorectal cancer**. This included a meta-analysis of seven cohort studies, giving a summary effect estimate of 0.96 (95% CI: 0.92 – 1.00). In their report it was noted that additional cohort studies were published after the analyses were conducted, but this did not change their overall judgement. Geelen et al. (2007), within the framework of the WCRF report in 2007, conducted a meta-analysis of prospective cohort studies published up to January 2006, addressing association between fish consumption, or n-3 fatty acids and colorectal cancer incidence and mortality. The pooled RR for colorectal cancer incidence (4559 cases of colorectal cancer) was 0.88 (95% CI 0.78 – 1.00) and for mortality 1.02 (95% CI 0.92 – 1.03).

Huxley et al. (2009) updated previous meta-analyses (including Geelen et al. (2007), see above) and gave a quantitative overview of the relationship between different lifestyle factors (alcohol, diabetes, red meat, processed meat, obesity, smoking, physical activity, fruits, vegetables, fish and poultry) and the risk of **colorectal cancer**. They included in total 103 cohort studies published between 1966 and January 2008 (Embase and Medline). They concluded with no apparent association between risk of colorectal cancer and consumption of fish (5317 cases on colorectal cancer, RR=0.93; 95% CI: 0.84, 1.04). (Engeset et al., 2007) reported no significant association in the Norwegian Women and Cancer study, which was included in the meta-analysis with 63914 women, of which 254 cases of colon cancer.

Randi et al. (2010) summarised papers addressing dietary patterns and the risk of **colorectal cancer**, and found that favourable dietary patterns for reducing cancer risk were mainly characterised by high consumption of fruits and vegetables, fish and poultry, and whole grains. It is possible that this is a result from fish replacing meat as a dietary protein source (Chan and Giovannucci, 2010). The association between red meat consumption and colorectal cancer is according to WCRF *convincing* (WCRF, 2007).

Xu et al. (2013) analysed colorectal risk with intake of white meat (poultry and fish) intake. The meta-analysis of 11 observational studies (case-controls and cohorts) for the high versus low consumption analysis of **colorectal adenoma** risk with fish intake gave an effect size estimate of 0.98 (95% CI 0.80-1.19) with low heterogeneity across studies (Xu et al., 2013). The authors concluded that fish consumption is not associated with colorectal adenoma risk.

Wu et al. (2012b) concluded that the results from their meta-analysis of fish consumption and **colorectal cancer** risk suggest that fish consumption is associated with lower risk of colorectal cancer. The study included relevant studies (22 cohorts and 19 case-control studies) identified by Medline and Embase up to May 2011. The pooled OR of colorectal cancer for the highest vs lowest fish consumption was 0.83 (95% CI 0.72-0.95) in case-control studies (with significant heterogeneity) and 0.93 (95% CI 0.86-1.01) in cohort studies.

4.4.4 Other cancers

Li et al. (2011) performed a meta-analysis including five cohorts and nine case-control studies on the association of fish consumption with urinary **bladder cancer** (including ureter and renal pelvis). The authors reported no significant decreased risk of these cancers (relative risk 0.86; 95% CI: 0.61, 1.12) with increased fish consumption. There was significant heterogeneity across the studies, and this could not be explained by study design, geographical region or method of exposure assessment.

Bai et al. (2013) conducted a meta-analysis of fish consumption and **renal cancer**, including 12 case-control studies and three cohort studies conducted between 1990 and 2011 (9324 cases, 608753 participants). The authors followed the PRISMA (preferred reporting items for

systematic reviews and meta-analyses) and MOOSE (meta-analysis of observational studies in epidemiology) guidelines. They found no association (RR=0.99; 95% CI: 0.92, 1.07).

Qin et al. (2012) found no association between fish consumption or LCPUFA intake and **pancreatic cancer** risk in a meta-analysis and systematic review. The paper included nine cohorts (n=1209265, 3082 cancer events) and 10 case-control studies (2514 cases and 18779 controls), and covered papers identified by PubMed and Embase up to February 2012.

Kolahdooz et al. (2010) concluded in a study on meat and fish consumption and **ovarian cancer** risk that low consumption of processed meat and higher consumption of poultry and fish may reduce the risk. The review and meta-analysis included eight studies on fish consumption with a pooled RR of 0.84 (95% CI 0.68-1.03). The papers were extracted with Medline and Embase up to November 2009 and the meta-analysis was conducted according to MOOSE guidelines.

Hosnijeh et al. (2014) investigated dietary intakes and risk of **leukaemia** (lymphoid and myeloid) in the EPIC cohort (n=477325, which includes 35170 women from Norway). During a mean follow up time of 11 years, 34773 leukaemia cases were identified. There were no significant associations between fish consumption and risk of leukaemia.

4.4.5 Contaminants in fish and cancer

Evidence based on occupational or accidental exposures at high doses and experimental animal studies show that dioxins can cause a variety of adverse health effects, including cancer. No studies specifically addressing contaminants in fish and cancer development were identified by the literature search.

The report of the joint FAO/WHO expert consultation on the risks and benefits of fish consumption concluded that there is *insufficient* evidence (Table 4.1) for adverse health effects (e.g. endocrine disruption, immunological and neurodevelopmental effects, cancer) associated with exposure to dioxins from fish consumption (FAO/WHO, 2011). However, epidemiological studies show that dioxins are carcinogenic at much higher exposure levels than obtained by dietary exposure from fish consumption. The WHO expert consultation concluded that potential cancer risks associated with dioxins are well below established coronary heart disease benefits from fish consumption.

4.5 Fish consumption and type-2 diabetes and metabolic outcomes

Association between fish consumption and type-2 diabetes or other metabolic outcomes were not addressed in the VKM benefit-risk assessment of fish consumption in 2006. In 2012 the Norwegian Directorate of Health did not directly address associations between fish consumption and type-2 diabetes, but referred to reports from WHO on protective associations between intake of marine n-3 PUFA and type-2 diabetes (WHO, 2003), and a

large prospective cohort study (Djousse et al., 2011) indicating increased risk of type-2 diabetes with increased intake of marine n-3PUFA.

From the literature search conducted by VKM, 14 papers addressing fish consumption and type-2 diabetes were selected for review in full-text. Seven of these are referred to in the summary below of more recent papers on fish consumption and risk of type-2 diabetes or other metabolic outcomes. The reviews and meta-analyses included the study by Djousse et al. (2011) mentioned above.

4.5.1 Type-2 diabetes mellitus

We identified six recent meta-analyses addressing fish consumption and incidence of **type-2 diabetes mellitus (T2DM)**, all restricted to prospective cohort studies (Wallin et al., 2012; Wu et al., 2012a; Xun and He, 2012; Zheng et al., 2012b; Zhou et al., 2012; Zhang et al., 2013). Zhang included studies to May 2013, whereas the other five included studies up to January – December 2011. Although these meta-analyses comprised over-lapping (but not identical) studies, their overall conclusions were partly conflicting.

Wu et al. (2012a) covered 16 prospective studies (18 separate cohorts, 540184 participants, of them 25670 cases) addressing relations of dietary n-3 PUFA, dietary fish and/or seafood, and n-3 PUFA biomarkers in humans with incidence of T2DM. Quality of included studies was assessed by predefined criteria. The study showed that consumption of fish and/or seafood was not associated with DM (n=13 studies, RR per 100g/day: 1.12; 95% CI: 0.94, 1.34). Substantial heterogeneity among studies was however observed. Study location (Asia vs North America/Europe), mean BMI and duration of follow-up modified the association between fish/seafood consumption and T2DM risk. Lower risk was seen in studies from Asia, in studies with lower mean BMI (less than 24.5 kg/m²), and in studies with shorter durations of follow up (less than 10 years). However, the independent effects of these factors could not be determined due to limited statistical power and high colinearity, and the authors concluded that the reasons for this (true biological heterogeneity, publication bias or chance) deserve further investigation.

Wallin et al. (2012) included 13 studies addressing total and/or oily fish consumption and three addressing only fatty acids (in total 527441 participants, 24082 diabetes cases) and found large heterogeneity between different continents (Europe, Asia/Australia, USA). Therefore, results across all studies were not combined into an overall summary risk estimate. They concluded that the risk of T2DM is not significantly associated with one serving per week increment of total fish consumption in Europe, but found an increased RR in the US, and reduced risk in Asia/Australia. Studies were however also partly inconsistent within study areas.

Xun and He (2012), in the same issue of Diabetes Care as the paper by Wallin et al. (2012), reported based on nine studies on fish consumption, including 438214 individuals, that they found no support for an overall inverse association between fish consumption and incidence

of T2DM (RR=0.99; 95% CI: 0.85, 1.16). In agreement with Wallin et al. (2012), they reported geographical heterogeneity. The divergent associations observed by Wallin et al. (2012) and Xun and He (2012) were also discussed in a commentary in the same issue of Diabetes Care Wylie-Rosett et al. (2012).

Zheng et al. (2012b) searched Chinese databases in addition to PubMed, EmBase, and Cochrane library for prospective studies on fish/seafood/n-3 PUFA exposure and incidence of T2DM, and results were reported according to PRISMA guidelines. Of the included 24 studies, seven reported association between fish intake and T2DM risk, 10 studies reported associations with n-3 PUFA intake and T2DM risk, and five studies reported both fish intake and n-3 PUFA intake in association with T2DM risk. The authors reported no association between total fish intake (highest vs lowest category, RR=1.07; 95% CI: 0.91, 1.25) or n-3 PUFA intake (RR 1.07, 95%CI 0.95 - 1.20) and risk of T2DM. Stratification into lean fish, oily fish and shellfish intake did not modify the conclusion. They observed high degree of heterogeneity, and subgroup analysis indicated reduced risk of T2DM with increased fish consumption and n-3 PUFA intake in Asian populations.

Zhou et al. (2012) included 10 papers on 13 cohorts in a meta-analysis. The study quality was assessed using the nine star Newcastle-Ottawa scale, and all included studies ranged from six to seven stars. In the highest versus lowest category analyses, the pooled RR of type-2 diabetes for intake of fish was 1.146 (95% CI 0.975 - 1.346, involving 367757 subjects) and for intake of n-3 fatty acids 1.076 (95% CI 0.955 - 1.213, involving 506665 subjects). Based on statistically significant linear dose-response trends for fish intake (involving three publications, five cohort studies) and n-3 fatty acids (involving four papers, six cohort studies) the authors concluded that higher fish consumption (nine cohorts, 367757 subjects) might be associated with a weak increase in T2DM risk, These authors also reported substantial between-study heterogeneity, but did not address geographical heterogeneity.

Zhang et al. (2013), the most recent meta-analysis, found no significant effect of fish/seafood (10 studies, 549955 participants, pooled RR=1.04; 95% CI: 0.9, 1.2) or marine n-3 LCPUFA intake (six studies, 346710 participants, pooled RR=1.08; 95% CI: 0.9, 1.3) on risk of T2DM, but observed a significant protective effect of oily fish intake (four studies, pooled RR=0.89; 95% CI: 0.82, 0.96). They also observed significant study heterogeneity with no obvious sources.

Of notice, all the above mentioned meta-analyses concluded that further investigation is warranted.

Patel et al. (2012) reported that results from the EPIC-InterAct Study, addressing fish consumption and T2DM in eight European countries (not Norway), showed a weak inverse association with oily fish consumption, and no association with lean fish, shell fish or total fish consumption. This study was included in the most recent meta-analysis (Zhang et al., 2013).

Rylander et al. (2014) published recently results from a prospective study on T2DM risk in 33740 participants in the Norwegian women and cancer study (NOWAC), and this study is not included in any of the meta-analyses above. The participants (mainly residing in the north and west of Norway) had no self-reported T2DM or history of stroke, angina or heart attack at inclusion in 1996-1998, when the mean age was 47.9 years. At follow up 6-9 years later, 479 participants reported diabetes. The overall prevalence was 2.6%, and the age-adjusted incidence rate per person years was 2.41 (95% CI 2.20-2.63). Mean intake of total fish was 93 g/day, dominated by fish products (mean 37 g/day) and lean fish (mean 29 g/day). Mean oily fish intake was 15 g/day. After confounder adjustment they found that lean fish consumption was inversely associated with T2DM compared to zero intakes and the decreased risk was dose-related. The rate ratio (RR) (95% CI) for 75 g lean fish/day was 0.71 (0.51-0.98). Although the RR for intake of total fish, oily fish and fish products was less than 1, it had no statistical significant effect on T2DM. The authors stressed that it was unclear whether lean fish in itself had a protective effect on T2DM, or that lean fish consumers have a protective life style that could not be taken into account in the study. However, unfavourable effects of fatty fish consumption or cod liver oil were not observed.

4.5.2 Overweight and metabolic syndrome

Jakobsen et al. (2013) investigated the associations between fish consumption and subsequent change in body weight among participants in the EPIC study (n=344757, including 10 European countries, among them Norway) that were followed for a median of five years and concluded that fish consumption (total and lean or fatty fish separated) has no appreciable association with body weight gain. In line with this, a previous publication from the EPIC study (n=89432, from five European countries, not including Norway, (Jakobsen et al., 2012) concluded that fish consumption did not prevent increase in waist circumference. A small study (n=109) on healthy adolescent Danish girls and boys reported positive association between red blood cell DHA concentration (an indicator of n-3 LCPUFA intake) and blood pressure and plasma insulin, which was contrary to what was expected (Lauritzen et al., 2012).

4.5.3 Contaminants in fish and type-2 diabetes and other metabolic outcomes

The literature search described in Chapter 4.1 identified no studies addressing fish consumption in relation to contaminant exposure from fish and association with type-2 diabetes and other metabolic outcomes. A workshop in 2011 on role of environmental chemicals in the development of diabetes and obesity which was organised by the US National Toxicology Program concluded that there is support for positive associations between type-2 diabetes and certain chlorinated POPs (Taylor et al., 2013).

4.6 Fish consumption and asthma, allergy and other atopic diseases

Association between fish consumption and allergic/atopic diseases was not addressed in the VKM benefit-risk assessment of fish consumption in 2006. Allergy to fish was discussed by VKM in 2006. Results in a report from the National Register of Severe Allergic Reactions to Food in 2011 show that reactions to fish are rare in the period from 2000 to 2010 (Namork et al., 2011). Allergies to different fish species are not further addressed in this report.

Studies addressing associations between fish consumption and asthma, allergy in general and other atopic diseases are summarized below.

Three meta-analyses addressing fish consumption and allergic/atopic diseases were identified by the literature search (Chapter 4.1.1).

Kremmyda et al. (2011) systematically reviewed **atopy risk** in infant and children in relation to early life exposure to fish. The search strategy and inclusion/exclusion criteria were not described in the paper, and the review did not address strength and weaknesses of the studies included. All five epidemiological studies (three prospective cohorts with total n=4315, one retrospective cohort with n=998, and one case-control study with 279 cases and 412 controls) investigating maternal fish consumption during pregnancy concluded with protective associations with the investigated outcomes (asthma, atopy, eczema, IgE, skin prick test, hay-fever). Regarding fish consumption in childhood and different atopic outcomes (skin prick test, asthma, wheeze, persistent cough, allergic rhinitis, hay fever, eczema allergic dermatitis, IgE, food allergy) the review included 14 studies with different study design (prospective cohorts, retrospective case-control, case-controls, cross sectional). Nine of 14 studies reported that fish consumption was protective against atopic outcomes in infants/children. Three studies did not observe associations, and two studies showed increased risk of atopy with higher fish consumption. The review concluded that the evidence is inconsistent, although a number of studies would support a protective effect of fish consumption.

Hooper et al. (2010) used a meta-analytic approach to identify dietary patterns common to different European countries in relation to current **asthma, asthma symptoms and bronchial responsiveness**. Two patterns emerged, one associated with intake of meats and potatoes, the other with fish, fruit and vegetables. There was no evidence that any of these patterns were related with the outcomes.

Yang et al. (2013) performed a systematic review and meta-analysis of prospective cohort studies up to December 2012 on fish intake in relation to **risk of asthma**. Based on three studies on infant fish consumption (total n=9212, of them 471 cases) the meta-analysis concluded with a protective association with fish consumption (RR=0.75; 95% CI: 0.61, 0.94). Two of the studies were from Norway (Nafstad et al., 2003; Oien et al., 2010) and the third from Sweden (Kull et al., 2006). Regarding two cohort studies on adult fish

consumption (total n=4687, of them 551 cases), no association was seen (RR=0.75; 95% CI: 0.69, 1.18) in the meta-analysis. The studies on maternal fish consumption and risk of asthma in offspring could not be pooled, but none of the two included studies indicated significant associations.

Some additional studies have been published after the above-mentioned reviews and meta-analysis.

Magnusson et al. (2013) recently published a 12 years follow up study of children in the Swedish BAMSE study (results in 4-year-olds presented in (Kull et al., 2004), and included in (Yang et al., 2013)). Their main finding was that children who consumed fish at 1 year had a dose-dependent overall reduced risk of prevalent **asthma, rhinitis and eczema** up to age 12 years. Adjusting for fish intake at age eight years did not change the results, and fish consumption at eight years was not associated with allergic disease at 12 years. In order to avoid influence of disease-related modification of exposure, since early onset of allergic disease delayed the introduction of fish in the child's diet, the analyses were also restricted to children without symptoms of allergy the first year of life. The associations were then attenuated, but still present, for rhinitis (OR=0.63; 95% CI: 0.46, 0.87, p-trend<0.001) and eczema (OR= 0.74; 95%CI: 0.52, 1.03, p-trend 0.008), but not for asthma (OR= 0.81, 95%CI: 0.48, 1.37, p-trend 0.303). The BAMSE study included 4089 newborns, and the blood samples from 2470 children (60%) were analysed for different IgE antibodies at 12 years of age.

Maslova et al. (2013) addressed maternal fish consumption and the risk of **asthma and child rhinitis** (doctor diagnosis reported by the parents) at 18 months and seven years in the Danish National Birth Cohort (n=28936). Mothers taking fish oil during the pregnancy were excluded. Never eating fish was associated with a higher risk of reported asthma at 18 months (n approximately 22000, OR= 1.30; 95%CI: 1.05, 1.63), but not with recurrent wheeze or allergic rhinitis. At seven years (n approximately 17000), high versus no maternal fish consumption during pregnancy was protective against early and ever asthma, but not against rhinitis. When early childhood fish intake, which was only modestly associated with maternal fish intake, was included in the analyses there was a slight attenuation of the effect estimates, but this did not alter the conclusion.

4.6.1 Contaminants in fish and asthma/allergy/atopy

The literature search described in Chapter 4.1 did not identify any studies addressing fish consumption in relation to contaminant exposure from fish and association with asthma/allergy/atopy.

4.7 Fish consumption and pregnancy related outcomes; other than neurodevelopment

VKM (2006) concluded that no negative effects of various nutrients and contaminants on growth and development of the foetus and infants were found after the use of n-3 fatty acids as a food supplement during pregnancy or as an addition to breastmilk during the post natal period. The increased intake of n-3 fatty acids seems to exercise a positive effect on the visual function of premature babies.

The benefit-risk assessment of VKM from 2006 did not address birth size and other pregnancy related outcomes. However, the literature search described in Chapter 4.1 identified studies from Norway that are relevant in the present report and these are summarised below.

4.7.1 Birth size

Leventakou et al. (2014) concluded that in a study with pooled and harmonised individual data from 19 European birth cohort studies (n=15188 mother-child pairs), moderate fish intake (fish consumption more than one but less than three times per week) during pregnancy is associated with lower risk of preterm birth (RR=0.87; 95% CI: 0.82, 0.92) and a small, but significant increase in birth weight (8.9 g; 95% CI: 3.3, 14.6 g). Women with more frequent fish consumption (more than three times per week) gave birth to children with higher weight (15.2 g; 95% CI: 8.9, 21.5 g). The association was greater in smokers and in overweight and obese women. A sub-study with 13 of the cohorts indicated that the associations were strongest for oily fish. This conclusion differs from that seen when data from the Norwegian MoBa study (62099 mother-child pairs) were analysed separately (Brantsaeter et al., 2012). Here it was found that lean fish was positively associated with birth weight, length and head circumference (adjusted beta for birth weight 0.45 g; 95% CI: 0.16, 0.65) while fatty fish was not associated with any of the birth size measures (adjusted beta for birth weight 0.04 g; 95% CI: -0.22, 0.26). For total fish the adjusted estimate for birth weight was 0.27 g, 95% CI: 0.12, 0.42). The relative risk of giving birth to a small baby (less than 2500 g) in full-term pregnancies was significantly lower in women who consumed more than 60 g/day of seafood than in women who consumed 5 g or less per day (OR= 0.56; 95% CI: 0.35, 0.88) (Brantsaeter et al., 2012).

4.7.2 Fish consumption and exposure to contaminants in relation to birth size

Papadopoulou et al. (2013) investigated the associations between maternal dietary intake of dioxins and PCBs during pregnancy and **birth size** in the Norwegian MoBa study (n=50651). As explained above, fish consumption shows positive association with fetal growth in this cohort, but is also the main dietary source of dioxins and PCBs. Seafood contributed on average to 41% of the dioxins and the dl-PCBs intake in the study population, but a low

proportion (2.2%) of the women had intakes of dioxins and dl-PCBs above the TWI of 14 pg TEQ/kg bw/week. In confounder-adjusted analyses, infants of mothers in the upper quartile of dioxins and dl-PCBs intake had lower birth weight (-62 g; 95% CI: -73, -50g), shorter birth length (-0.26 cm; 95%CI: -0.31, -0.20 cm) and shorter head circumference (-0.10 cm; 95% CI: -0.14, -0.06 cm) than infants of mothers in the lowest quartile of intake. The negative association was however weaker as seafood consumption was increasing. There was no statistically significant association between intake of dioxins and PCBs and the risk for having a small for gestational age neonate.

As described before, seafood is the main contributor to dietary mercury exposure. Vejrup et al. (2014) reported the association between maternal dietary exposure to mercury and infant **birth weight** in the Norwegian MoBa study (n= 56 988). Women in the highest quintile of mercury intake had infants with lower birth weight (-34 g; 95% CI: -46,-22 g) than women in the lowest quintile. Furthermore, they had an increased risk of giving birth to small-for-gestation-age offspring (OR=1.19; 95% CI: 1.08, 1.30). Although seafood intake was positively associated with birth weight, there were negative associations between Hg intake and birth weight within each of four strata of seafood intake. Only 10 of the women had calculated dietary intake of mercury above 1.6 µg/kg bw/week, indicating that a very low proportion had an intake above the TWI of 1.3 µg/kg bw/week which set by EFSA in 2012 (EFSA, 2012a).

4.7.3 Other pregnancy related outcomes

Haugen et al. (2011) reported that in a study on 7710 pregnant women in the Norwegian MoBa cohort, being in the upper tertile of seafood consumption in the year prior to the index pregnancy was associated with a lower risk of developing **hyperemesis gravidarum** (severe nausea and vomiting in early pregnancy) than being in the lower tertile (OR=0.56; 95% CI: 0.32, 0.98)

4.8 Summary of health effects associated with fish consumption

Since publication of the VKM report from 2006 (VKM, 2006), several extensive observational studies and intervention studies have been conducted, addressing beneficial and/or adverse effects of fish and EPA plus DHA supplementation on specific health outcomes in the general population and/or specific subgroups. Different population and specific cohort studies have systematically been reviewed by scientists as well as national and international health authorities with focus on one or several health outcomes. Thus, at present, the knowledge-base for assessing health effects associated with fish consumption is considerably strengthened.

VKM conducted two searches on literature published between 2009 -2014. VKM has not systematically weighted the evidence from national and international comprehensive reports, reviews/meta-analyses and individual studies, but summarised the results. Single studies from the Nordic region were included because they were considered of special relevance. In

addition, single studies published in 2014 were included in order to cover the most recent information.

In this summary of health effects associated with fish consumption, VKM has aimed at integrating the most important conclusions from both the assessments done by the national and international health authorities (FAO/WHO, EFSA, the Norwegian National Council for Nutrition) as well as relevant data retrieved from the present literature search of epidemiological studies on fish consumption and specific health outcomes. The assessments from the international health authorities mainly address possible association with fish consumption and cardiovascular disease and optimal neurodevelopment, since these are most thoroughly addressed in previous research. However, more information was available also on cancer, type 2 diabetes, atopic disease and pregnancy related endpoints than in the VKM assessment in 2006.

4.8.1 Fish consumption and cardiovascular diseases

The reviews, meta-analyses and other cohort or population-based studies, that have been summarised address fish consumption and n-3 fatty acids (EPA and DHA) from fish and the same or different type of end point for cardiovascular disease. The studies, however, may differ in the tools used for the estimation of fish consumption, in the tools used to measure the particular cardiovascular outcome of interest, and in the adjustment for confounding variables. The heterogeneity of the epidemiological studies thus hampers quantitative risk-benefit analyses of fish consumption and risk of a particular cardiovascular outcome.

Cardiac mortality

With regard to this health outcome, the reviews, meta-analyses and other cohort or population-based studies summarised in the present VKM opinion reinforce the conclusions of VKM (2006), FAO/WHO (2011), the Norwegian National Council for Nutrition (2011) and EFSA (2014b), that there is strong evidence or *Convincing evidence* (FAO/WHO) in humans that fish consumption and marine n-3 fatty acids reduce the risk of cardiac mortality in adults. The beneficial effect is observed at 1-2 servings of fish up to 3-4 servings per week. No benefit is found at higher intakes (more than 5 servings per week). The dose-response relationship appears to be non-linear. However, the limited number of high and very high fish consumers in these epidemiological studies does not allow for drawing firm conclusions about the actual balance of risk and benefit at these high intakes. The health benefits of fish on cardiac mortality are most likely due to EPA and DHA, however, the nutritional impact of fish consumption may be higher than the sum of the benefits of the individual nutrients consumed separately. Despite some conflicting findings in reviews and meta-analyses regarding the effect of supplementary EPA and DHA on cardiovascular diseases, new scientific evidence does not imply a change in the previously established beneficial effect of supplementary EPA and/or DHA in prevention of cardiac death.

Based on the conclusions from VKM (2006), FAO/WHO (2011), the Norwegian National Council for Nutrition (2011), EFSA (2014b), and the studies summarised in this report on fish consumption and cardiac mortality, VKM concludes that there is strong evidence in humans that fish consumption and EPA plus DHA reduce the risk of cardiac mortality in adults. VKM acknowledges that this effect is observed at relatively low fish consumption, 1-2 servings of fish per week, and up to 3-4 servings per week. Furthermore, VKM notes that the calculated benefits of fish consumption in relation to cardiac mortality refer to net effects combining beneficial, neutral, and adverse effects of nutrients and non-nutrients, including contaminants such as methylmercury, dioxins, dl-PCBs. VKM also notes that EPA and DHA play an important role, however, the beneficial effects of fish intake on cardiac mortality risk are most likely mediated through a complex interplay among a wide range of nutrients commonly found in fish, fat or lean.

Other cardiovascular outcomes

EFSA (2014b) only assessed cardiac death as cardiovascular health outcome. With regard to other cardiovascular health outcomes, the reviews, meta-analyses and other cohort or population-based studies summarised in the present VKM Opinion reinforce the conclusions of FAO/WHO (2011) that there is also *emerging or probable evidence* that fish consumption may reduce the risk of multiple other adverse cardiovascular health outcomes, including ischaemic stroke, non-fatal heart disease events, congestive heart failure and atrial fibrillation. The beneficial effect of fish consumption on the different outcomes being stronger among those who had moderate (2-4 servings per week) than dose who consumed low amounts (1 serving or less per week). The dose-response relationship appears to be non-linear since consumption of more than 4 servings per week gave no additional health effect. In a pooled analysis based on five prospective studies evaluating associations between fish intake and incident heart failure, Djousse et al. (2012) concluded that an inverse dose dependent relationship between fish consumption and EPA plus DHA with heart failure incidence exist, and that fish intake of 1-4 servings per week is associated with a risk reduction of up to 15% compared to less than 1 serving of fish per week. Furthermore results from recent cohort or population-based studies, particularly from Scandinavia, (results a.o. that consumption of fish, especially lean fish may reduce risk of stroke in women in a cohort of Swedish women), concluded that the beneficial effects of fish intake on cerebrovascular risk might be mediated through a complex interplay among a wide range of nutrients commonly found in fish, fat or lean.

VKM supports the conclusions of FAO/WHO (2011) and the studies summarised in this report on fish consumption and other cardiovascular outcomes, and concludes that the beneficial effect of fish consumption on the risk of multiple other adverse cardiovascular health outcomes, including ischaemic stroke, non-fatal coronary heart disease events, congestive heart failure and atrial fibrillation being stronger among those who had moderate (2-4 servings per week) than those who consumed low amounts (1 serving or less per week). Dose-response is

non-linear. VKM acknowledges that a dose dependent inverse relationship between fish consumption and EPA plus DHA with heart failure incidence exists; fish intake 1-4 servings per week is associated with a risk reduction of up to 15% compared to less than 1 serving of fish per week.

All the studies referred above have demonstrated that consumption of fish may be associated with beneficial effects even though contaminants are present in the fish consumed. Very few studies have examined the influence of beneficial effect of fish taken into account the contaminants present. When balancing the benefits of fish consumption on cardiovascular disease with the risk from contaminants such as PCBs, dioxins and methylmercury in fish, the outcome may be affected by the contaminant exposure.

FAO/WHO (2011) concluded that in the general adult population there is an absence of *probable or convincing evidence* of risk of coronary heart disease associated with methylmercury. The mercury opinion from EFSA in 2012 concluded that the observations related to mercury exposure and myocardial infarction, heart rate variability and possibly blood pressure are of potential importance, but still not conclusive.

Recent cohort or population-based studies, particularly from Scandinavia state that exposure to methylmercury is associated with increased risk of myocardial infarction (MI), and higher sum marine n-3 PUFA serum concentrations are associated with decreased risk of MI in a combined Swedish and Finnish population. This indicates that n-3 LCPUFA may be more beneficial if mercury exposure from fish consumption was lower. However, few studies on beneficial effects on fish take contaminant exposure into consideration.

VKM acknowledges that the net benefit of fish consumption on cardiovascular disease is affected by the concentrations of methylmercury.

4.8.2 Fish consumption and neurodevelopmental outcomes

The reviews, meta-analyses and other cohort or population-based studies that have been summarised, address fish consumption and n-3 fatty acids (EPA and DHA) from fish and the same or different type of end point for neurodevelopment. The studies, however, may differ in the tools used for the estimation of fish consumption, in the tools used to measure the particular neurodevelopmental health outcome of interest, and in the adjustment for confounding variables. Thus, the heterogeneity of the epidemiological studies makes quantitative risk-benefit analyses of fish consumption and neurodevelopmental outcomes challenging.

In 2006, a positive association between fish consumption and n-3 fatty acids during pregnancy and neurodevelopmental health outcomes was indicated. The reviews, meta-analyses and other cohort or population-based studies summarised in the present VKM Opinion reinforce the the conclusions made by FAO/WHO (2011) and EFSA (2014b) that there is significant positive associations (*convincing evidence*, FAO/WHO) between fish/seafood consumption and EPA plus DHA intake during pregnancy and children's

neurodevelopment. The beneficial effects are observed at fish/seafood consumption of about 1-2 servings per week and up to 3-4 servings per week compared to no fish/seafood consumption, and there appears to be no additional benefit with higher fish consumption. However, the limited number of high and very high fish consumers in these epidemiological studies does not allow for drawing firm conclusions about the actual balance of risk and benefit at these high intakes.

Based on the conclusions from FAO/WHO (2011), EFSA (2014b) and the studies summarised in this report on fish consumption and neurodevelopmental outcomes, VKM concludes that there is significant positive associations between fish consumption and EPA plus DHA intake during pregnancy and children's neurodevelopment. VKM acknowledges that this association is observed at relatively low fish consumption of about 1-2 servings per week and up to 3-4 servings per week compared to no fish/seafood consumption. VKM also notes that the calculated benefits of fish consumption in relation to neurodevelopmental outcomes in fetuses and infants refer to fish/seafood per se, including nutrients (e.g. DHA, iodine) and contaminants (such as methylmercury, dioxins and dl-PCBs) contained in fish/seafood. Furthermore, VKM also acknowledges that the observed health benefits of fish consumption during pregnancy on neurodevelopment may depend on the maternal status with regard to nutrients and the contribution from fish relative to other sources of nutrients essential for neurodevelopment.

VKM also notes the results from a recent quantitative assessment published by the US Food and Drug Administration of the net effects on foetal neurodevelopment of eating fish during pregnancy (FDA, 2014). As large approximations were necessary to fit the data, VKM agrees with EFSA (EFSA, 2014b) that quantitative benefit assessments are generally hampered by the heterogeneity of the studies.

All the studies referred above have demonstrated that consumption of fish may be associated with beneficial effects even though contaminants are present in the fish consumed. There are few studies that have examined the influence of beneficial effect of fish taken into account the contaminants present. A single study from the Faroe Islands show negative confounding by EPA and DHA on the associations between mercury exposure and neurodevelopmental endpoints. Indication of such effect has also been reported from the Seychelles, and was taken into account when the TWI for methylmercury was set (EFSA, 2012a).

VKM acknowledges that high exposure to methylmercury may reduce the beneficial effect of fish consumption on neurodevelopment.

Other health outcomes related to the central nervous system

Several observational studies, intervention studies and experimental studies have investigated the potential role of EPA and DHA found in fatty fish to prevent and treat

cognitive decline and Alzheimer's disease. Conflicting results have been published, and the evidence for beneficial effect of fish consumption and cognitive decline or Alzheimer's disease is weak.

4.8.3 Fish consumption and cancer

In 2007 WCRF concluded with limited-suggestive evidence that fish protects against colorectal cancer. Meta-analyses published since 2009 do not find associations between fish consumption and colorectal cancer risk.

Meta-analyses published since 2009 summarising studies that measure fish consumption as g fish/day or the number of servings per week, show no association with risk of cancer in the urinary bladder, kidneys, stomach, intestines, pancreas, breast, ovaries or prostate.

VKM concludes that meta-analyses conducted since 2009 do not show association between fish consumption and cancer. None of the studies controlled for contaminant exposure from fish, and it is not known whether this would have affected the outcome.

4.8.4 Fish consumption and type-2 diabetes and other metabolic outcomes

Results from six reviews and meta-analyses published since 2009 indicate that there are no strong associations between fish consumption and type-2 diabetes. However, there is large regional heterogeneity between studies, and no firm conclusions can be drawn.

From the Nordic countries, a new study on Norwegian women show a reduced risk of developing type-2 diabetes with increasing lean fish consumption, and no indications of unfavourable effects of fatty fish consumption. A study in Finnish middle-aged and old men showed reduced long-term risk of type-2 diabetes with increasing serum concentration of EPA, DHA and DPA.

VKM concludes that the studies summarized have not revealed strong associations between fish consumption and type-2 diabetes, although some Nordic studies indicate protective associations. None of the studies controlled for contaminant exposure from fish and it is not known whether this would have affected the outcome.

No conclusions can be drawn based on the few prospective studies on fish consumption and weight increase identified in the literature search conducted by VKM.

4.8.5 Fish consumption and asthma, allergy and other atopic diseases

The majority of cohort studies addressing atopic diseases indicate a protective association with maternal fish consumption and/or early life fish consumption. There is little evidence for any association between fish consumption later in childhood or adulthood and atopic disease.

VKM concludes that the studies indicate a protective association between maternal fish consumption and/or early life fish consumption and atopic diseases. None of the studies controlled for contaminant exposure from fish and it is not known whether this would have affected the outcome.

4.8.6 Fish consumption and pregnancy related outcomes

Most of the studies included from the literature search came from the Norwegian MoBa cohort. VKM notes that one study reported that women with high fish consumption during the year previous to pregnancy had a lower risk of developing severe nausea and vomiting in early pregnancy.

Results from MoBa indicate that fish consumption during pregnancy, and in particular lean fish consumption, is associated with increased birth weight and lower risk of preterm birth. Studies also indicate that prenatal exposure to both mercury and dioxins and PCBs can decrease birth weight. VKM concludes that this implies that the overall beneficial effect of fish consumption on birth weight might have been more beneficial in the absence of contaminants, and that the findings need to be confirmed in other cohorts.

5 Changes in farmed Atlantic salmon feed composition – the significance for nutrients and contaminants in the fillet

Over the last 10 years there has been a dramatic change in raw materials used in fish feeds (Ytrestøyl et al., 2014). Since 2006 the production of farmed Atlantic salmon and trout has increased dramatically followed by the same percentage of increase in volumes of feed produced (Figure 5-1). Fish feed volumes have increased but the fish meal and fish oil available for feed production have remained constant (Figure 5-2). Hence, new raw materials have increasingly replaced fish meal as a protein source and fish oil as a lipid source (Figure 5-3). Thus far plant proteins and vegetable oils are the alternative ingredients, accounting for 70% of the feed in 2013 (Shepherd and Jackson, 2013), (Global Production by production source 1950-2011, Release date: March 2013).

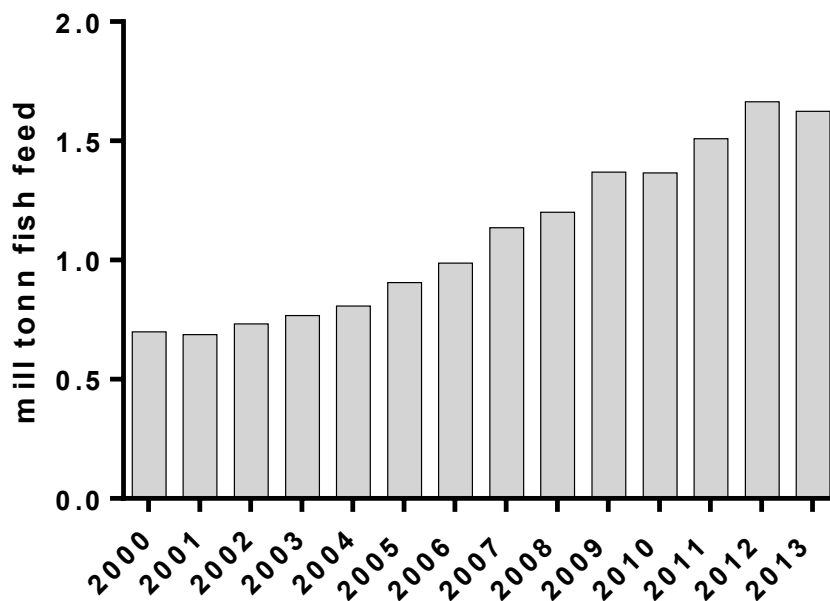


Figure 5-1 Fish feed used in Norwegian fish farming from 2000 to 2013. Numbers are in million tonnes. Source: Biomass Statistics of the Norwegian Directorate of Fisheries, updated June 2014.)

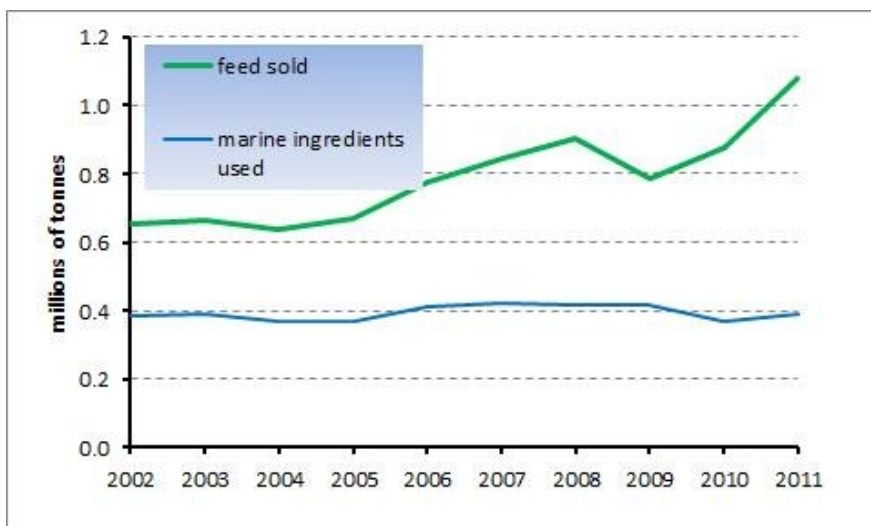


Figure 5-2 An example from one of the large fish feed companies in Norway with their own figures on a stable use of marine ingredients concomitant with about a two-fold increase in tonnes of fish feed produced. Source: www.ewos.com

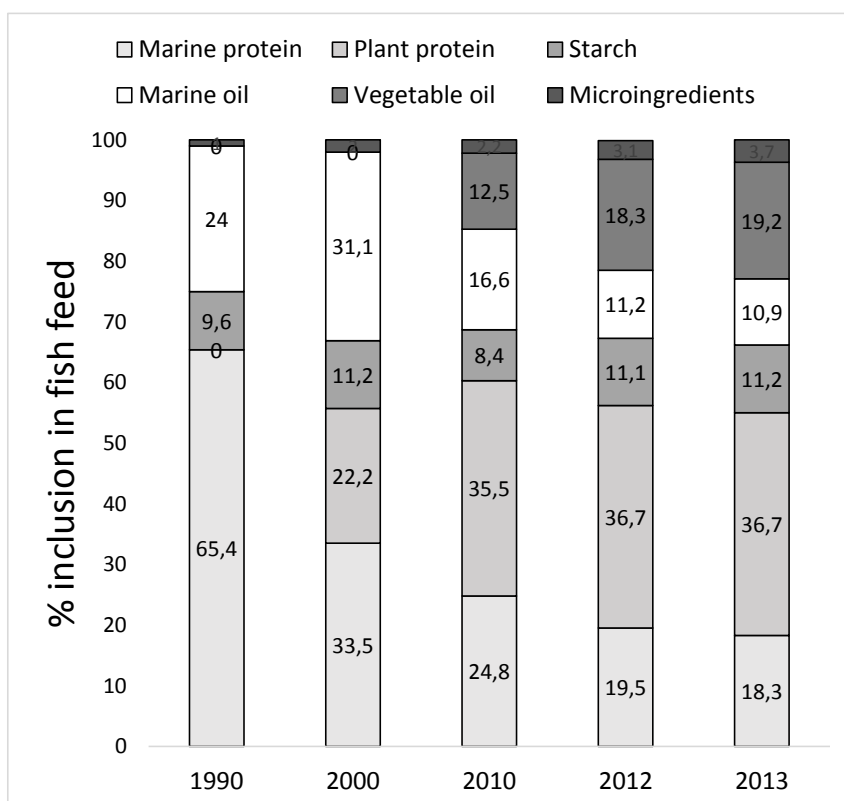


Figure 5-3 Development of ingredients in commercial fish feed over the past 20 years in Norwegian aquaculture. Numbers on the bars indicate the percent of the ingredients. Source: Ytrestøyl et al. (2014)

The total oil inclusion in farmed Atlantic salmon feed increased from 23.4% oil as fish oil in 1990 to approximately 30% oil as fish oil in 2000 (Figure 5-3). From 2000 to 2010 the feed oil source changed and approximately 40% of the oil was the vegetable oil rapeseed oil

(Figure 5-3). The clear trend for fish feed development is decreased fish oil and fish meal levels, and it is expected that future feeds for farmed Atlantic salmon and trout contain lower amounts of fish oil and hence lower amounts of EPA and DHA. Ultimately, the farmed fish own nutrient requirements for EPA and DHA will set the minimum possible EPA and DHA content of fish feed. Future feeds for farmed fish is also expected to contain new raw materials as alternatives to plant proteins and vegetable oils.

When replacing the raw materials fish meal and fish oil with plant ingredients as protein and lipid sources, also a range of other nutrients and undesirable components will change. In this chapter, we present the changes of nutrients and contaminants in fish feed for Norwegian farmed Atlantic salmon and trout. Further, time-trends for the same nutrients and contaminants in Norwegian farmed Atlantic salmon and trout is shown, and any changes in fillet composition are seen in relation to changes in the feed content from 2006 until farmed fish harvested in 2013. The main bulk of data is extracted from two surveillance programs financed by Norwegian Food Authorities and carried out by NIFES (Annual Feed surveillance program and 93/23 annual surveillance of farmed fish). Annual reports from both surveillance programs are available at www.matilsynet.no and www.nifes.no. Emerging risks with changes of fish feed raw material composition is also included in this chapter.

5.1 Nutrients in feed and farmed fish

5.1.1 Alternative protein ingredients in fish feed

Fish and other seafood are recognised as an important source of animal protein with balanced amino acid profile. The balance of amino acids is optimal for human requirement of essential amino acids, and seafood protein is easily digestible due to low amount of connective tissue. Typically fish fillet contain 15 to 20 g protein per 100 g fillet on wet weight basis, thus varying much less than the lipid content. Fish fillet, similar to other animal protein sources, do not contain any significant amount of carbohydrates.

Irrespective of which raw material that provides the dietary amino acids for the fish, the fish muscle protein composition will remain the same. Hence, there are no difference in fillet amino acid composition when comparing salmon from 2006 and 2014. Plant protein sources commonly used in fish feeds are legumes. Soybean is dominating, but options of using other beans and peas are continuously being investigated. Legumes also contain anti-nutrients; these latter are thoroughly described by VKM (2009). None of the anti-nutrients present are identified to be transferred to the fish fillet, and are therefore not considered any further in the present report. In 2013, regulations opened the possibility to use processed animal proteins (PAPs) in feed for salmon (Hatlen et al., 2014; Liland et al., 2014). These protein sources (from poultry and swine) have a more similar amino acid profile compared to fish proteins, and does not contain the anti-nutrients as found to challenge fish health when plant proteins are used. Still, for the consumer, the salmon muscle protein is exactly the same independent of feed protein source. Replacing marine proteins with plant proteins will probably introduce new contaminants, such as pesticides (Chapter 5.3).

5.1.2 Fatty acid levels and profiles

The use of high-lipid feeds for cultured fish may affect fish flesh quality by increasing the percentage of lipids stored in the edible muscle (Arzel et al., 1993; Arzel et al., 1994; Bendiksen et al., 2003; Hemre and Sandnes, 1999; Watanabe, 1982). Generally, increased dietary lipid resulted in increased fillet lipid levels, whereas changing dietary fatty acid composition by replacing fish oil with a vegetable oil blend, did not change the amount of total body lipid stores in Atlantic salmon (Nanton et al., 2007).

Globally, the inclusion of vegetable oils in aqua feeds as a replacement for fish oil is increasing. In contrast to fish, vegetable oils and terrestrial animal fats are lacking in n-3 LCPUFA, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), and are characterised by a low to very low n-3/n-6 ratio. As reviewed by Turchini and co-workers (Turchini et al., 2009), a number of studies have shown that the complete or partial dietary replacement of fish oil with vegetable oils or a vegetable oil blend affects the fatty acid composition of the edible portion.

Replacing fish oil with vegetable oils in fish feed results in increased content of the plant fatty acids linoleic acid (LA), oleic acid (OA) and alpha-linolenic acid (ALA), and decreased content of EPA, DPA (docosapentaenoic acid) and DHA both in fish whole body, various organs and fillet. However, the magnitude of fatty acid change is dependent on the type of tissue (Bell et al., 2001; Bell et al., 2003; Torstensen et al., 2004) and the amount of phospholipids (PL) relative to neutral lipids in the tissue. The storage triacylglycerol (TAG) fraction (neutral lipids) of the lipids of different tissues more closely resembles the fatty acid make-up of the diet than does the structural PL fraction.

Fatty acid composition of the diets is reflected in the fatty acid compositions of the fish muscle in almost all species studied. However, the positive correlation observed for the other fatty acids is not that obvious for saturated fatty acids (Kennish et al., 1992; Mugrditchian et al., 1981; Turchini et al., 2003; Viola et al., 1981). It has been demonstrated that saturated fats are deposited into fish fillet at a specific physiological level and being less dependent on dietary level. For example, Atlantic salmon fed up to 50% saturated fatty acids by using palm oil as dietary oil, did not increase the level of saturated fat in salmon fillet beyond the maximum of 25% seen in fish oil fed salmon (Bell et al., 2002; Torstensen et al., 2000).

It is clear that when fish oil is replaced by vegetable oil, the most significant modifications of the fatty acid composition of fish tissues are increased C₁₈ PUFA content (particularly the n-6 fatty acid linoleic acid; Figure 5.1.2-1), decreased EPA, DPA and DHA content and a modification of the monounsaturated (MUFA) composition from C₂₀ and C₂₂ MUFA to C₁₈ MUFA. For these reasons, the content of linoleic acid (18:2 n-6) in an alternative lipid source is one of important parameters to be considered, as an increase in this fatty acid contribute to the decrease in n-3/n-6 ratio and increase in total n-6. As illustrated by Figures 5.1.2-1 and 5.1.2-2 the content of EPA+DHA has gradually decreased whereas total n-6 has gradually increased in Atlantic salmon fillets due to a shift in raw materials from only fish meal and fish oil to more vegetable oils, and especially rapeseed oil replacing fish oil. Fish

feed EPA, DHA and n-6 levels are not analysed and given in detail in the same time period, hence only fish fillet concentrations are presented in this report.

The gradual replacement of fish oil with vegetable oils in commercial fish feed is also reflected in the ratio between n-3 and total n-6 in fish feed decreasing from 4.7 in 2006 to 1.6 in 2013 (Sanden et al., 2014). The feed surveillance program reported EPA+DHA fish feed levels of 3.2% EPA+DHA in the feed in 2012 (n=23) and 2.5% EPA+DHA in the feed in 2013 (n=69) (Sanden et al., 2014), whereas n-6 were 3.1% of the feed in 2012 and 3.4% of the feed in 2013 (Sanden et al., 2014). The replacement of fish oil with vegetable oils of commercial fish feed was also reflected in the Norwegian Atlantic salmon fillet EPA+DHA content (Fig. 5.2-1) and n-6 content (Figure 5.1.2-2). The fatty acid DPA was not included in Figure 5.1.2-1. Hence, all the figures are 15 to 20% lower compared to the total EPA+DPA+DHA sum. The reason for illustrating EPA+DHA in fish fillet is to be able to compare directly with dietary intake recommendations, which refer to EPA and DHA. In addition, studies on human health effects of n-3 mainly refer to EPA and DHA intakes, and only occasionally to DPA intake.

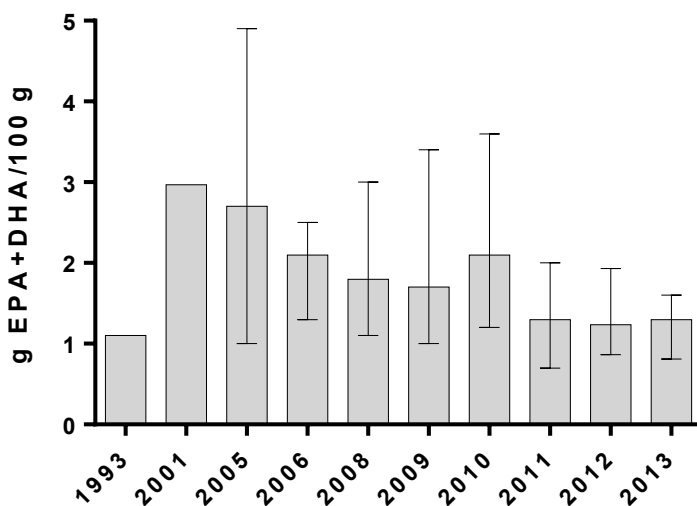


Figure 5.1.2-1 Atlantic **salmon fillet content** of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (g/100 g fillet) from 1993 to 2013 presented as mean with lowest and highest measured value. Numbers of sampled fish per year were: n=1 (pooled sample) (1993); n=1 (pooled sample) (2001); n=47 (2005); n=10 (2006); n=28 (2008); n=28 (2009); n=33 (2010); n=100 (2011); n=100 (2012); n=90 (2013). Source: www.nifes.no/sjomatdata

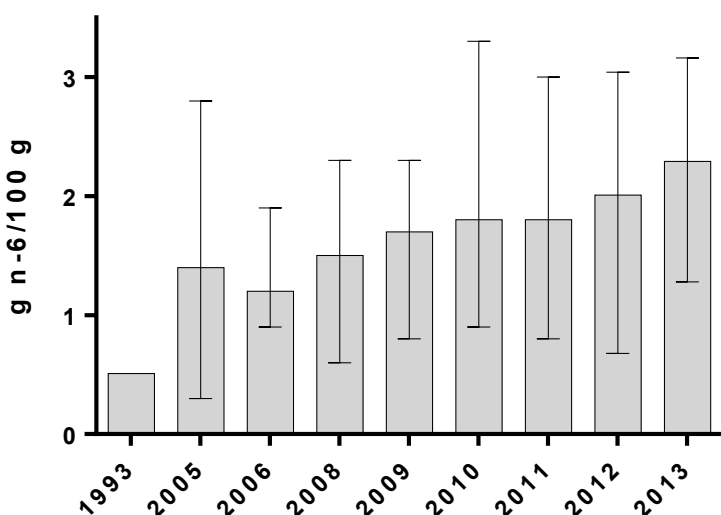


Figure 5.1.2-2 Atlantic **salmon fillet content** of n-6 fatty acids (g/100 g fillet) from 1993 to 2013 presented as mean with lowest and highest measured value. Numbers of fish per year were: n=1 (1993, pooled sample); n=1 (2001, pooled sample); n=47 (2005); n=10 (2006); n=28 (2008); n=28 (2009); n=33 (2010); n=100 (2011); n=100 (2012); n=90 (2013). Source: www.nifes.no/sjomatdata.

5.1.3 Vitamin D

Atlantic salmon is regarded as a good source of vitamin D (measured as vitamin D₃). In 2006 the commercial fish feed held quite high levels of marine ingredients which naturally contained high vitamin D levels. With steadily decreasing use of marine ingredients and increasing use of alternatives, vitamin D₃ levels in fish feed has decreased during the last decade as shown in data obtained from the Norwegian fish feed surveillance program (Figure 5.1.3-1) (Sanden et al., 2014; Sissener et al., 2013). There is no data on Atlantic salmon fillet vitamin D content during the same time period. However, as Atlantic salmon fillet vitamin D content reflects the feed levels of vitamin D₃ (Horvli et al., 1998), it is expected to be decreased compared to the content in 2006.

Farmed Atlantic salmon harvested in 2012 contained an average of 0.06 mg vitamin D per kg fillet with a range of 0.002 to 0.18 mg per kg. This is a 25% decrease in Norwegian farmed Atlantic salmon fillet since 2006 when the average vitamin D content was reported to be 0.08 mg per kg, ranging from 0.04 mg/kg to 0.16 mg/kg (www.nifes.no; seafood data, (VKM, 2006). However, since the content of vitamin D in the fillet reflects the fish feed vitamin D₃ content (Graff et al., 2002), replacing marine ingredients with plant based material will further decrease the feed vitamin D₃ content and thus fillet vitamin D content.

Cleaning fish oil for marine contaminants will also remove vitamins D, E and A from fish oil, which may be a concern for the vitamins A and D, which cannot be restored in fish feed due to legal restrictions.

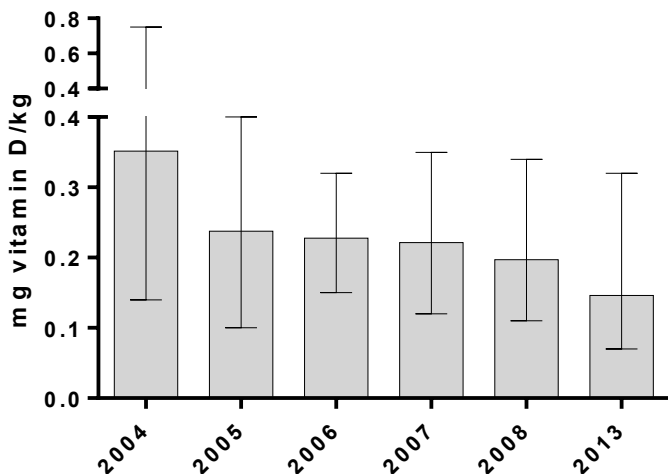


Figure 5.1.3-1 Fish **feed content** of vitamin D₃ (mg/kg feed) in the period from 2004 to 2013 presented as mean with lowest and highest measured value. Numbers of feed samples per year were: n=21 (2004); n=20 (2005); n=20 (2006); n=22 (2007); n=21 (2008); n=69 (2013). Source: Sanden et al. (2014)

5.1.4 Selenium and iodide in feed and farmed Atlantic salmon

The feed surveillance program years 2000-2014, provides information on contents of selenium and iodine in feed (Sanden et al., 2014).

Mean fish feed selenium levels have decreased with approximately 50% since 2006, and today's mean selenium levels are 0.7 mg/kg feed (Sanden et al., 2014). Maximum limit of selenium allowed to add to feed is 0.5 mg/kg, which limits the possibility to add selenium back to former high selenium levels above 1.2 mg selenium/kg feed experienced with high fish meal and fish oil based feed (Figure 5.1.4-1).

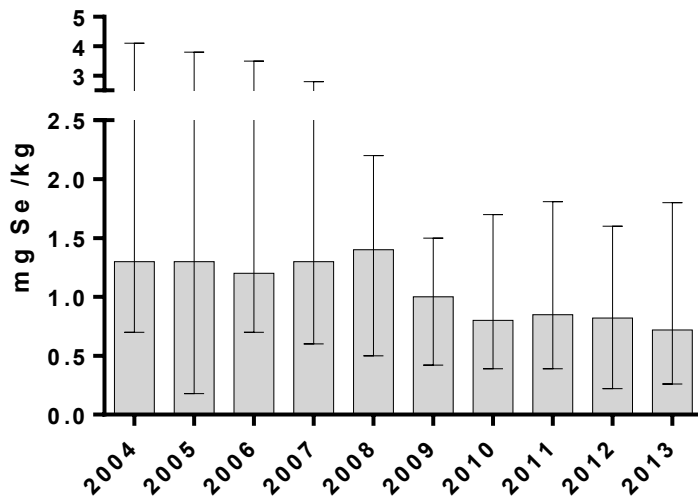


Figure 5.1.4-1 Fish **feed content** of selenium (Se) (mg/kg feed) in the period from 2004 to 2013 presented as mean lowest and highest measured value. Numbers of feed samples per year were: n=40 (2004); n=23 (2005); n=49 (2006); n=22 (2007); n=21 (2008); n=69 (2013). Source: Sanden et al. (2014)

Farmed Atlantic salmon fillet is regarded as a good source of selenium. Figure 5.1.4-2 shows that the reduction in selenium in the feed has resulted in reduced Atlantic salmon fillet concentrations (Sanden et al., 2014). A further decrease in feed and Atlantic salmon fillet selenium content is a likely scenario if plant protein sources lower in bioavailable selenium than fish meal increase any further.

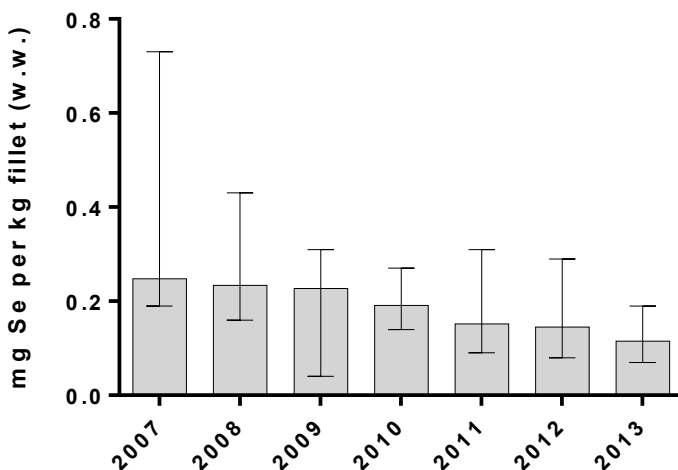


Figure 5.1.4-2 Atlantic **salmon fillet content** of selenium (Se) (mg/kg fillet) in 2007-2013 presented as mean with lowest and highest measured value. Each sample analysed is a pooled sample of five fish. Numbers of pooled samples per year were: n=135 (2007); n=131 (2008); n=148 (2009); n=148 (2010); n=301 (2011); n=305 (2012); n=132 (2013). Source: www.nifes.no/sjomatdata.

Farmed Atlantic salmon is not regarded as a good source for iodine. There has been a steady decline in iodine level in fish feed from just above 4 mg iodine per kg in 2004 to just above 2 mg iodine per kg in 2007 (Sanden et al., 2014), likely due to decreased fish meal inclusion. In 2007-2013 the fish feed iodine levels however, have remained relatively constant at 2.2 mg/kg (Sanden et al., 2014). For seawater fish the main source of iodine is the surrounding water (direct uptake through gills and intestine). The iodine concentration (mainly in the forms of iodide and iodate) in the sea varies between 0.44 and 0.49 $\mu\text{mol/L}$, which is high enough to satisfy the fish's iodine requirement. No data showing time-trends from 2006 to 2013 for farmed Atlantic salmon and trout fillet iodine levels have been found.

In the human diet, salmonids, such as Atlantic salmon and trout, are not considered as any major sources of dietary iodine. Wild lean fish like cod and saithe, are regarded as good dietary iodine sources.

5.2 Contaminants in feed and farmed fish

When the use of feed raw materials have changed from fish meal and fish oil to other sources as described above, the content of POPs and heavy metals has decreased significantly as presented in detail below for dioxins, dl-PCBs and mercury. In addition, the content of PCB-6 and new risks introduced by new raw materials are described below.

The data presented are taken from the annual surveillance programs for fish feed (Sanden et al., 2014) and farmed fish (Hannisdal et al., 2014). The data are presented as mean with the variation showing the lowest and highest measured values for each year. The samples are randomly collected during the whole year, and originate from different fish farms and fish feed producers. Hence, it is not possible to identify differences in data variations observed within each year.

5.2.1 Dioxins and dioxin-like-PCBs

Overall, the surveillance of commercial **fish feed** shows a substantial reduction in marine POP's including dioxins and dioxin-like (dl) PCBs (Figures 5.2.1-1 and -2) which follows the change in inclusion levels of fish oil from early 2000 until 2014 (Sanden et al., 2014; Sissener et al., 2013). The data on **fillet levels** of dioxins and dl-PCBs from Norwegian commercial Atlantic salmon show a similar decrease from 2004 to 2013, Figure 5.2.1-3;(Hannisdal et al., 2014). Hence, the mean upper bound concentration of sum dioxin and dl-PCBs was 0.5 ng TEQ per kg fillet in 2012 and 2013 compared to 1.5 ng TEQ per kg fillet in 2006.

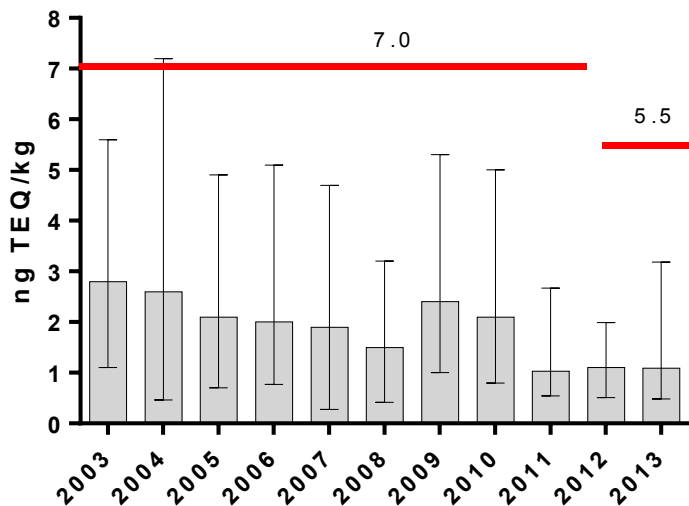


Figure 5.2.1-1 Fish **feed content** of dioxins and dioxin-like PCBs (dl-PCBs) presented as as upper bound mean total toxicological equivalents (total TEQ) in the period from 2003 to 2013, with lowest and highest measured value (µg/kg feed). Upper bound imply that concentrations lower than the limit of detection or limit of quantification is substituted with the actual value of these limits and not zero, which most likely represent an overestimate of the true values. Current and previous maximum limits of total TEQ permitted in fish feed are marked with a red line. Source: (Sanden et al. (2014); Sissener et al. (2013))

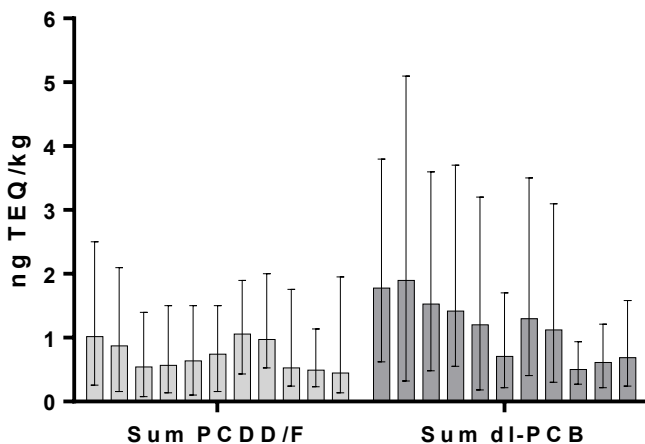


Figure 5.2.1-2 Fish **feed content** of sum dioxins (PCDD/F) and dioxin-like PCBs (dl-PCBs) in 2013 given as upper bound mean total toxicological equivalents (2005-TEQ) with lowest and highest measured value (µg/kg feed). Upper bound imply that concentrations lower than the limit of detection or limit of quantification is substituted with the actual value of these limits and not zero, which most likely represent an overestimate of the true values. Source: Sanden et al. (2014)

As illustrated in Figure 5.2.1-2, sum dl-PCBs and sum dioxins have decreased in a similar manner in fish feed, however the decrease has been 10 percent points greater for the dl-PCBs compared to the dioxins. Hence, in fish feed the total sum of dioxins and dl-PCBs TEQ

has decreased with 60%. Of this, total sum dl-PCBs TEQ has decreased 61% and sum dioxin TEQ has decreased 51% from 2003 to 2013. In today's fish feed, the dioxins and dl-PCBs contribute more equal amounts to the total sum TEQ compared to the composition 10 years ago when dl-PCBs was dominating over sum dioxins (Figure 5.2.1-2). Interestingly, fish feed levels of sum dioxins and dl-PCBs was higher in 2009 and 2010 compared to the previous years 2007 and 2008 (Figure 5.2.1-1). This was reflected in a 2010-exception of the steadily and gradual decreasing Atlantic salmon fillet dioxin and dl-PCBs content (Figure 5.2.1-3). As prices of raw materials are fluctuating, lower prices of fish oil in the time period 2009-2010 resulted in higher fish oil inclusion in fish feed and thus higher levels of dioxins and dl-PCBs in fish feed and Atlantic salmon fillets during this period. After 2010, however, the fish oil levels have generally decreased in fish feed for Norwegian farmed Atlantic salmon and trout due to the increased production volume and unchanged fish oil volumes available on the global markets. This is reflected in the lowest content of dioxins and dl-PCBs measured in fish feed during this time period (1.09 ng TEQ per kg fish feed in 2013).

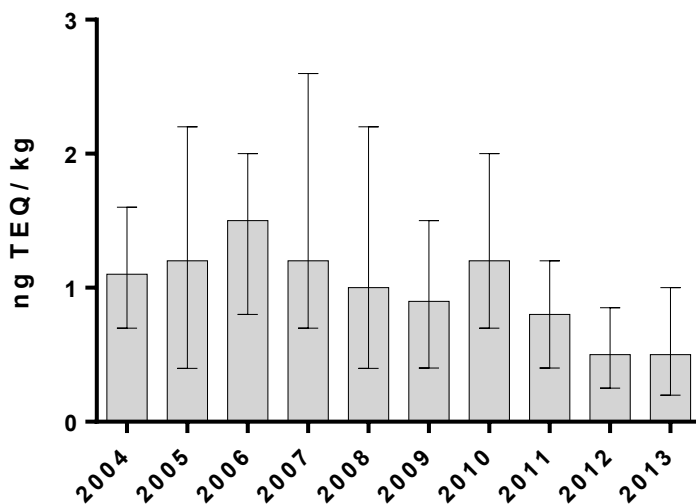


Figure 5.2.1-3 Norwegian farmed Atlantic **salmon fillet contents** of dioxins and dioxin-like (dl-PCBs) in the period from 2004 to 2013 given as total toxicological equivalents (2005-TEQ; ng/kg fillet). Values are upper bound mean with minimum and maximum. Upper bound imply that concentrations lower than the limit of detection or limit of quantification is substituted with the actual value of these limits and not zero, which most likely represent an overestimate of the true values. Numbers of pooled samples of five fish each per year were: n=40 (2004); n=155 (2005); n=125 (2006); n=580 (2007); n=430 (2008); n=270 (2009); n=183 (2010); n=140 (2011); n=155 (2012); 105 (2013). Source: www.nifes.no/sjomatdata

Research has revealed that both dioxins and dl-PCBs are reflected in Atlantic salmon fillet depending on the level in the feed (Berntssen et al., 2005). Farmed Atlantic salmon and farmed trout surveillance data, showing a decline in sum dioxins and dl-PCBs from 2006 until 2013 (Figures. 5.5.1-3 and -4), confirm this. Nøstbakken et al. (2015) have demonstrated that the decline in sum TEQ per kg fillet in farmed salmon is statistically significant. Since 2006, the content of dioxins and dl-PCBs in farmed Atlantic salmon has decreased 67%

down to 0.5 ng TEQ per kg fillet in 2013. For farmed trout, the concentration was the same as farmed Atlantic salmon in 2012 and 2013 (Figure 5.2.1-4).

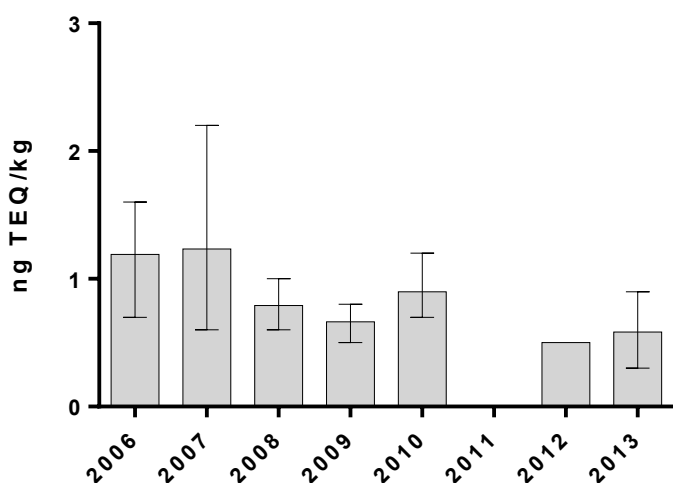


Figure 5.2.1-4 Norwegian farmed **trout fillet** contents of dioxins and dl-PCBs in the period from 2006 to 2013 given as total toxicological equivalents (2005-TEQ)(ng/kg fillet). Values are «upper bound» mean with minimum and maximum. Upper bound imply that concentrations lower than the limit of detection or limit of quantification is substituted with the actual value of these limits and not zero, which most likely represent an overestimate of the true values. All years each sample analysed was a pooled sample of five fish. Numbers of pooled samples per year were: n=10 (2006); n=12 (2007); n=10 (2008); n=8 (2009); n=4 (2010); n=0 (2011); n=1 (2012); n=16 (2013). Source: www.nifes.no/sjomatdata

Fish feed and Atlantic salmon fillet content of PCBs (Figs. 5.2.1-5 and -6) follow the same trend as dioxins and dl-PCBs (Figs. 5.2.1-1 and -2). Compared with 2006, PCB-6 in Atlantic salmon fillet decreased with more than 50% down to a mean concentration of 3.6 µg/kg fillet (Hannisdal et al., 2014). Since 2012, a maximum limit was implemented in Norway and EU of 40 µg/kg PCB-6 in fish feed (Commission Regulation (EU) No 277/2012 of the European Parliament and of the Council on undesirable substances in animal feed). The sum of PCB6 does not include PCB-118, which was previously included in the PCB-7 sum. Since 2012, PCB-118 is included as one of the congeners in the maximum limit of sum TEQ for dioxins and dl-PCBs.

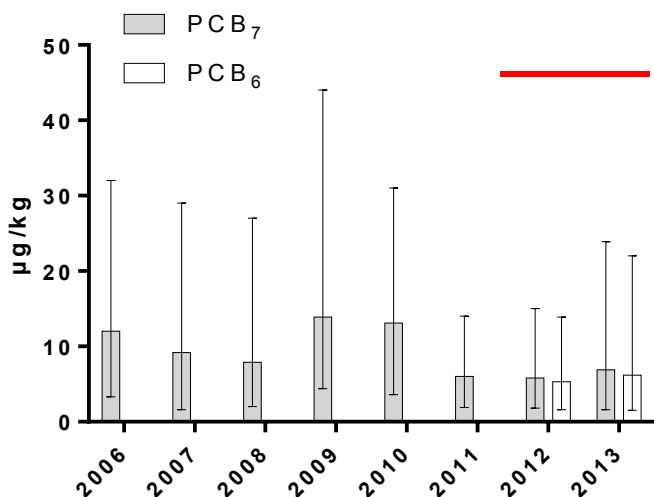


Figure 5.2.1-5 Fish **feed content** of sum PCB-6 and PCB-7 in the period from 2006 to 2013. Values are upper bound mean with minimum and maximum in µg/kg feed. The maximum limit for sum PCB-6 is marked with a red line (40 µg/kg). Upper bound imply that concentrations lower than the limit of detection or limit of quantification is substituted with the actual value of these limits and not zero, which most likely represent an overestimate of the true values. Numbers of feed samples per year were: n=54 (2006); n=57 (2007); n=57 (2008); n=25 (2009); n=23 (2010); n=25 (2011); n=23 (2012); n=69 (2013). Source: Sanden et al. (2014)

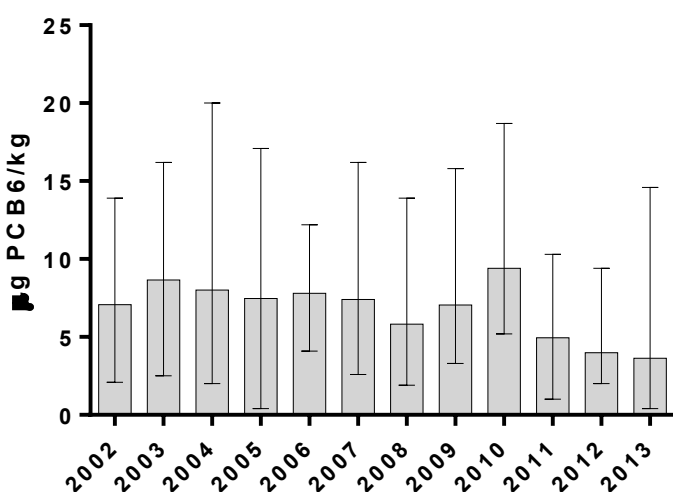


Figure 5.2.1-6 Norwegian farmed Atlantic **salmon fillet contents** of sum PCB-6 in the period from 2002 to 2013 presented as upper bound mean with the lowest and highest value (µg/kg fillet). From 2005, each sample analysed is a pooled sample of five fish, whereas samples before 2005 represent a mix of individual fish and pooled samples of five fish each. Numbers of pooled samples of five fish each per year were: n=32x (2002); n=37 (2003); n=36 (2004); n=36 (2005); n=19 (2006); n=92 (2007); n=89 (2008); n=52 (2009); n=32 (2010); n=70 (2011); n=77 (2012); n=205 (2013). Source: www.nifes.no/sjomatdata

5.2.1.1 Cleaned fish oil reduce persistent organic contaminants in farmed salmon

In addition to reducing persistent organic pollutants (POPs) in Atlantic salmon fish feed and fillet by replacing fish oil with vegetable oils, the fish oil can also be cleaned of POPs.

A number of physical-chemical refining methods can be used to remove fat-soluble contaminants such as dioxins, dl-PCBs and brominated flame-retardants from marine oils. Several methods exist that can potentially be used for this purpose, such as activated carbon (Maes et al., 2005; Oterhals et al., 2007; Usydus et al., 2009), steam deodorization/steam distillation (De Kock et al., 2004), thin-film deodorization, short path distillation (Breivik and Thorstad, 2005; Olli et al., 2013; Oterhals et al., 2010), super critical fluid extraction (Krukoniš, 1989). In addition, combination techniques are used such as active carbon followed by thin-film deodorization (Berntssen et al., 2010a; Berntssen et al., 2010b; Sprague et al., 2010), or countercurrent supercritical CO₂ extraction in combination with active (Kawashima et al., 2009).

Activated carbon effectively removes dioxins and non-ortho dl-PCBs from fish oil, but is less effective in removing mono-ortho-PCBs (Oterhals et al., 2007). Activated carbon does not remove PBDEs from fish oil. Short path distillation (also called molecular distillation) is, however, an effective method of removing dioxins, dl-PCBs, ndl-PCBs and PBDEs from oils (Oterhals et al., 2010; VKM, 2011a). However, when cleaning the oil efficiently for POPs this also affect the level of fat-soluble vitamins (depending on the process), but only to a minor extent affect the fatty acid profile (Oterhals and Berntssen, 2010). Removal of the contaminants mentioned here from fish meal requires totally different methods, which are based primarily on the removal of fat by organic solvent extraction and improved fat separation, or solid-liquid extraction (leaching) where the intermediate processed fishmeal is contacted with a triglyceride oil (Oterhals and Kvamme, 2013).

Two long-term feeding (more than 16 months) trials have been conducted where cleaned fish oil was used in feeds to Atlantic salmon (Berntssen et al., 2010b; Olli et al., 2010). In the first study, Atlantic salmon were fed a diet with a 100% inclusion of fish oil which was decontaminated with a short path distillation technique (Olli et al., 2010). In the second study, the diets were based on half plant oil and half fish oil (representing the salmon feed composition at that time) in which the fish oil was decontaminated with a combined active carbon and thin-film deodorization technique (Berntssen et al., 2010b; Lock et al., 2011). In a third short term trial (less than 3 months) (Sprague et al., 2010), salmon were fed a full fish oil diets in which the fish oils were decontaminated with the same combined active carbon and thin-film deodorization as in (Berntssen et al., 2010b). Finally in a fourth trial, a decontaminated finishing feed (6 months before slaughter) was fed to Atlantic salmon that previously were fed on a full fish oil diet. The oil was subjected to an activated carbon decontamination treatment (Bell et al., 2012). All studies efficiently removed POPs resulting in 76.6% reduction (2.31 vs 0.54 ng (2005 TEQ-WHO)/kg (Olli et al., 2010), 94% reduction (6.42 vs 0.34 1998 TEQ-WHO)/kg)(Sprague et al., 2010), 80.8% reduction (1.3 vs. 0.25 ng (1998 TEQ-WHO)/kg)(Berntssen et al., 2010b), and approximately 25% reduction (1.94 vs

approx. 1.45 (1998 TEQ-WHO)/kg) (Bell et al., 2012) in sum dioxins and dl-PCBs in fish fillets. These data are achieved by three different studies where Atlantic salmon were fed either feed with standard fish oil or cleaned fish oil. The lowest level of dioxins and dl-PCBs achieved by using cleaned fish oil was 0.25 ng TEQ (1998 TEQ-WHO)/kg Atlantic salmon fillet (Berntssen et al., 2010b).

5.2.1.2 Cleaned fish oil and Atlantic salmon nutrient composition

The cleaning process that removed more than 93% of the POPs in the fish oil Berntssen et al. (2010b) also removed lipid soluble vitamins but had only very minor effects on the fatty acid profile. How much vitamins that is lost in the cleaning process is however dependent on processing conditions and type of cleaning technique (Lock et al., 2011; Oterhals and Berntssen, 2010). Farmed fatty fish is traditionally good sources for vitamin D. In one long-term feeding trials with Atlantic salmon, the lipid soluble vitamins A, D and E were added to achieve fish oil-like concentrations in the fish feed (Lock et al., 2011), and no negative effects on fish fillet vitamin D concentrations or fish health were reported. In the long term trial of Olli et al. (2010), no supplies were made to compensate for potential vitamin loss and no negative effect was reported on fish health (vitamin levels were not reported). Lock et al. (2011) reported only a slight reduction in EPA and DHA in decontaminated oils and fish fed on these oils, whereas Olli and colleagues (2010) reported even an increased EPA and DHA concentration in cleaned fish oil fed fish, despite lower levels in the cleaned oil compared to the unprocessed oil. Although lipid soluble vitamins can be added from a practical point of view, current feed legislation hinders this for vitamin D. As discussed previously the maximum limit for vitamin D addition to fish feed is 0.075 mg/kg and far below the vitamin D concentrations added in the two referred experiments. Consequently, commercially produced Atlantic salmon with cleaned fish oil will have lower vitamin D fillet levels than Atlantic salmon fed non-cleaned fish oil.

5.2.1.3 Cleaned fish oil in fish feeds - modelling of the resulting concentrations of dioxins and dl-PCBs in Atlantic salmon fillet

The two feeding trials were performed with high fish oil inclusion levels (100% or 50% of oil source in diet), which are no longer relevant for present and future commercial fish oil inclusion levels (Figure 5-4). We have therefore calculated the expected concentrations of sum dioxins and dl-PCBs based on a scenario relevant for today's and future feeds where feed consists of 10% fish meal, 56% plant protein sources, 10% cleaned fish oil and 20% vegetable oil. The level of dioxins and dl-PCBs in the feed was determined by calculating the total sum dioxins and dl-PCBs contributed from fish meal, plant protein sources, cleaned fish oil and vegetable oils. The model published by Berntssen and Lundebye (2007), take into account the initial concentration of dioxins and dl-PCBs in the smolt at the start of a seawater production cycle, uptake and elimination rates of each dioxin and dl-PCBs, feeding rate, and growth of the fish. When using commercial relevant data for growth and data on dioxins and dl-PCBs in fish meal, plant protein sources and vegetable oils from the feed surveillance (Sanden et al., 2014), the calculated fillet concentration of sum dioxins and dl-

PCBs was 0.3 ng TEQ dioxins and dl-PCBs/kg fillet. One may expect that the dioxin and dl-PCBs levels would be even lower than the 0.25 ng TEQ dioxins and dl-PCBs/kg fillet in Atlantic salmon fed cleaned fish oil (15% of the feed) as reported by Berntssen et al. (2010b). However, in this trial the growth was much higher than is normally found under commercial conditions, thus giving lower final levels than the model predicted levels that uses lower but commercial relevant growth rates. When the model is run with growth rate and feed intake levels as found in the experimental trial of (Berntssen et al., 2010b), the model predicts levels of 0.23 ng TEQ dioxins and dl-PCBs/kg fillet which is close to the actual analysed levels of 0.25 ng TEQ dioxins and dl-PCBs/kg fillet. Please note that predicted levels of dioxins and dl-PCBs in fish fed cleaned fish oil will vary because of variation in the other feed ingredients contaminant concentrations, fish growth, initial contaminant concentrations and if data are given as upper bound, medium bound or lower bound concentrations of sum dioxins and dl-PCBs.

When the decontaminated fish oil is defined as the only source for dioxins+dl-PCBs and no initial smolt dioxins+dl-PCBs levels are given, the model predicts fillet levels of 0.06 ng TEQ dioxins and dl-PCBs/kg fillet. However, also the other feed ingredients will contribute with dioxins and dl-PCBs resulting in a higher minimum concentration level. The predicted concentrations presented here are in the same range as other fatty foods such as cheese (0.29 medium bound WHO-TEQ 2006 ng/kg product) and somewhat higher than beef (0.18 medium bound WHO-TEQ 2006 ng/kg product) (De Mul et al., 2008).

5.2.2 Mercury

Some industrial fish (e.g. blue whiting) used as marine feed ingredients are naturally high in mercury. Mercury is found primarily in organic form (75 to 95%), specifically as methylmercury which represent a potential health hazard (Chapter 2.3.1). The assimilation of methylmercury from feed to salmon is relatively high (23 to 41%), and the muscle is an important organ for storage (Berntssen et al., 2004). In 2013, the fish feed surveillance reported levels of mercury which ranged from 0.006 to 0.19 mg/kg with a mean of 0.03 mg Hg/kg feed (Sanden et al., 2014). This represents 50% reduction in total feed mercury levels compared to 2004-2006 values (Sanden et al., 2014; Sissener et al., 2013). Fish meal is the main source of Hg in fish feed, and the decline in total feed mercury is likely due to the decreased fish meal inclusion as protein source in fish feed (Figure 5.2.2-1). The maximum limit for mercury in feed is 0.1 mg/kg.

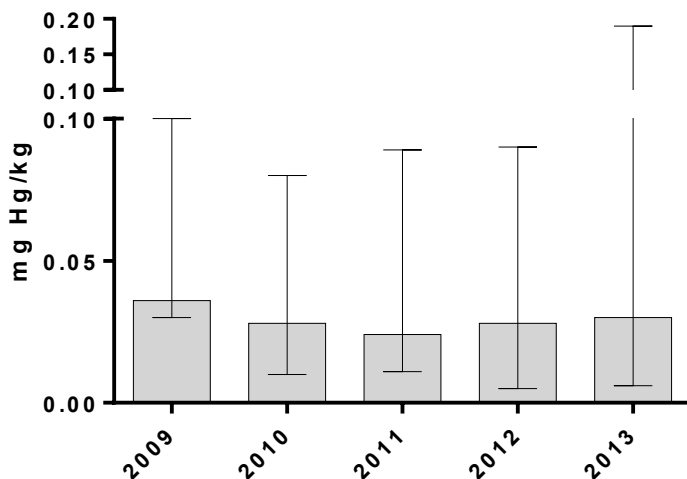


Figure 5.2.2-1 Fish **feed content** of total mercury (Hg) in the period from 2009 to 2013. Values are in mg/kg presented as upper bound mean with the lowest and highest value. Upper bound imply that concentrations lower than the limit of detection or limit of quantification is substituted with the actual value of these limits and not zero, which most likely represent an overestimate of the true values. Numbers of feed samples per year were: n=2 (2009); n=23 (2010); n=25 (2011); n=23 (2012); n=69 (2013). Source: Sissener et al. (2013)

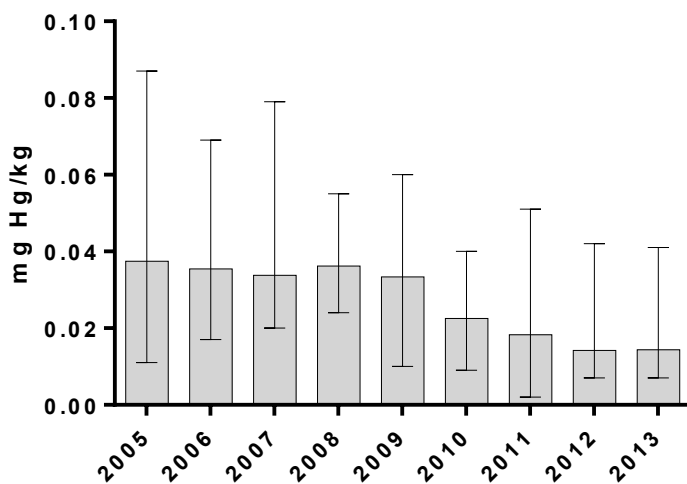


Figure 5.2.2-2 Norwegian farmed Atlantic **salmon fillet contents** of mercury (Hg) (mg/kg fillet) in the period from 2005 to 2013 presented as upper bound mean with the lowest and highest value. Upper bound imply that concentrations lower than the limit of detection or limit of quantification is substituted with the actual value of these limits and not zero, which most likely represent an overestimate of the true values. Each sample represents five fish. Numbers of pooled samples of five fish each per year were: n=26 (2005); n=104 (2006); n=149 (2007); n=137 (2008); n=148 (2009); n=121 (2010); n=300 (2011); n=305 (2012); n=132 (2013). Source: www.nifes.no/sjomatdata.

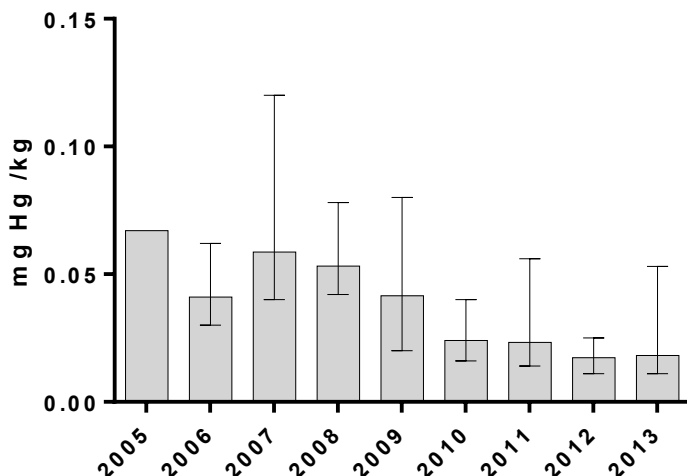


Figure 5.2.2-3 Norwegian farmed **trout fillet contents** of mercury (Hg) (mg/kg) in the period from 2005 to 2013 presented as upper bound mean with the lowest and highest value. Upper bound imply that concentrations lower than the limit of detection or limit of quantification is substituted with the actual value of these limits and not zero, which most likely represent an overestimate of the true values. Each sample represents five fish. Numbers of pooled samples of five fish each per year were: n=1 (2005); n=7 (2006); n=17 (2007); n=13 (2008); n=19 (2009); n=31 (2010); n=15 (2011); n=24 (2012); n=20 (2013). Source: www.nifes.no/sjomatdata

As expected, farmed Atlantic salmon and trout fillet Hg reflects the feed Hg decreases (Figures 5.5.2-2 and -3). The magnitude of decrease in mean fillet Hg content is similar for Atlantic salmon and trout (60% and 70%, respectively), and today's Norwegian farmed Atlantic salmon and trout have a mean Hg level of 0.014 mg per kg fillet and 0.018 mg per kg fillet, respectively. In the current exposure estimates (Chapter 7), data for farmed Atlantic salmon is used due to the very similar nutrient and contaminant concentrations. It is also difficult to differentiate between trout and salmon in the food consumption surveys.

5.2.3 Other persistent organic pollutants (POPs)/legacy POPs

In the 2006 report a thorough identification of hazards was done discussing a range of chemical contaminants which may be present in fish feed and fish. Since the 2006 report concluded that intake from marine organisms did not represent a significant health risk, these substances are not discussed further in this report as no new information has been identified which may change the conclusion on risk.

The substances relevant for fish feed are legacy POPs including pesticides which are not legal to use but is present in the environment. The concentrations in fish feed ingredients and fish feed is being monitored and regulated through maximum limits in animal and fish feed and feed raw materials. These include the two iso-forms of DDT (dichlor-difeny-trichlorethan) and its metabolites DDE and DDD, toxaphene (seven different toxaphene

components are annually monitored, i.e. toxaphene number 26, 50, 62, 32, sum toxaphene 40+41 and toxaphene 42), *cis*- og *trans*- chlordan plus *cis*- and *trans*- nonachlor and oksychlordan, aldrin and dieldrin, mirex, endrin, isodrin, hexachlorbenzene (HCB), heptachlor and heptachlor-endo-epoxide are all included in the annual feed surveillance and results from 2013 are recently reported by Sanden et al. (2014).

5.3 Emerging risks from new ingredients in fish feed

All feed ingredients contribute with unwanted substances. Replacing fish oil and fish meal with alternative ingredients decrease the levels of marine contaminants, however, the new ingredients may contribute with similar and/or other types of contaminants. Since today's aquaculture mainly replaces marine raw materials with plant proteins and vegetable oils, contaminants originating from these will be emphasised.

5.3.1 Pesticides from plant raw materials

The pesticides included in the feed surveillance are mainly the ones which are not legal to use any more (Chapter 5.5), but exist in the environment. In addition, legal pesticides are being used for crops all over the world, and residues can be present in plant protein and lipid raw materials. Raw materials for fish feed are purchased on the global market, and can therefore contain a range of pesticide residues. To date the knowledge of composition and concentration of pesticide residues in fish feed ingredients and fish feed are limited, but have recently been screened (Nacher-Mestre et al., 2014). Based on screening results, analyses of chlorpyrifos and pirimiphos-methyl have been included in the yearly Norwegian feed surveillance program (Sanden et al., ongoing surveillance; pers. comm.). Knowledge on transfer of these pesticides from feed to fish is lacking.

Current legislation on pesticides (396/2005) include 451 substances with maximum residue levels (MRL) for plant and land-produced food, however MRL for seafood and raw materials solely used for feed is not yet established.

Endosulfan is a pesticide on the Stockholm Conventions list of persistent organic pollutants and its use is being phased out. Endosulfan is not authorised in the European Union and is regulated as an undesirable substance in animal feed including fish feed. Endosulfan is still used in some parts of the world that export food and feed ingredients to Europe. The EU MRL for endosulfan in animal feed is 0.1 mg/kg, while the MRL in fish feed is 0.05 mg/kg (Commission Regulation (EU) No 744/2012). Surveillance of fish feed reports levels between 0.0006 and 0.001 mg endosulfan/kg in the last six years and in 2013 the average content was 0.0007 mg/kg (Figure 5.3.1-1). Surveillance of farmed Atlantic salmon reports low endosulfan levels in farmed Atlantic salmon with 0.006 mg endosulfan per kg fish fillet as the highest value measured in 2013 (Hannisdal et al 2014). There is currently no maximum residue level (MRL) in the European Union or Norway for endosulfan in farmed fish, but there is a MRL for endosulfan in meat at 0.1 mg/kg. Endosulfan exposure estimates from a daily consumption of 300 g farmed Atlantic salmon will constitute approximately 0.5% of the

acceptable daily intake (ADI) of 0.006 mg/kg bw/day for a person weighing 70 kg. ADI is the acceptable daily intake of e.g. a pesticide, that a person can be exposed to every day throughout life without representing health risk (see Glossary).

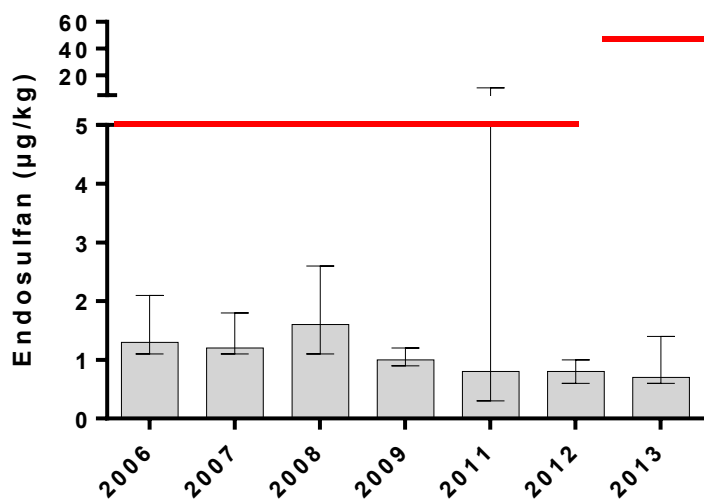


Figure 5.3.1-1 Fish **feed content** of sum endosulfan in the period from 2006 to 2013. Values are upper bound mean with minimum and maximum in µg/kg feed. Upper bound imply that concentrations lower than the limit of detection or limit of quantification is substituted with the actual value of these limits and not zero, which most likely represent an overestimate of the true values. The maximum limit is marked with a red line (currently 50 µg/kg which previously was 5 µg/kg). Number of feed samples per year were: n=20 (2006); n=20 (2007); n=21 (2008); n=24 (2009); n=0 (2010); n=25 (2011); n=23 (2012); n=69 (2013). Source: Sanden et al. (2014)

5.3.2 Synthetic antioxidants

Synthetic antioxidants are used as preservatives in fish feed ingredients to prevent auto-oxidation of unsaturated lipids in fish meal or fish oil. These include propylgallate (PG), butylhydroksyanisol (BHA), butylhydroksytoluen (BHT) and ethoxyquin (EQ) as laid down in EC 1831/2003. Ethoxyquin (EQ) is predominantly used in fishmeal and is a prerequisite for sea transport of fishmeal over long distances to avoid oxidation and the subsequent danger of self-ignition. BHT and BHA are predominantly used in fish oils and the maximum permitted level of these and other synthetic antioxidants is 150 mg/kg feed. The synthetic antioxidants were not assessed in the 2006 VKM report (VKM, 2006). However, public concern about negative health effects of synthetic antioxidants, in particular EQ, in seafood has led to public interest in this issue. The safety of synthetic antioxidants has been evaluated several times by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), the former European Commission's Scientific Committee for Food (SCF) and the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) in the case of EQ, since this compound is also used as a pesticide (JMPR, 2005). The European Food Safety Authority (EFSA) is currently re-assessing

all feed additives that have applied for re-authorisation and the European Commission has given EQ top priority.

In feed for Atlantic salmon, the concentration of synthetic antioxidants varies between years and do not seem to reflect the last years change in ingredient composition (Figure 5.3.2-1). Although synthetic antioxidants such as EQ can be found in plant ingredients (NIFES, unpublished data), the levels are low compared to in fishmeal.

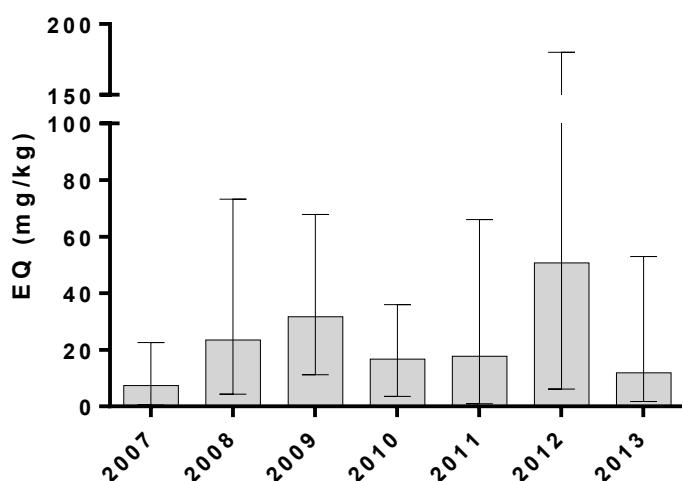


Figure 5.3.2-1 Fish **feed content** of ethoxyquin (EQ) in the period from 2007 to 2013. Values are upper bound mean with minimum and maximum in mg/kg feed. Upper bound imply that concentrations lower than the limit of detection or limit of quantification is substituted with the actual value of these limits and not zero, which most likely represent an overestimate of the true values. The maximum limit for EQ in fish feed is currently 150 mg/kg. Numbers of feed samples per year were: n=22 (2007); n=21 (2008); n=25 (2009); n=23 (2010); n=25 (2011); n=23 (2012); n=69 (2013). Source: Sanden et al. (2014)

There are currently no MRLs in the European Union for synthetic antioxidants in food products from farmed animals. In contrast, Japan has set MRLs of 10 mg BHT/kg, 1 mg EQ per kg and 0.5 mg BHA per kg for fish (Japanese Ministry of Health, Labour and Welfare www.mhlw.go.jp/english/). Lundebye et al. (2010) have calculated the intake of EQ, BHT and BHA from fillets from a number of farmed species (cod, salmon, halibut and trout) and showed that EQ can constitute between 4 and 15%, BHT can constitute between 34 and 74%, and BHA can constitute with less than 1% of their respective ADIs on daily consumption of a 300 g portion of fish. However, in 2012 EFSA re-evaluated the ADI of BHT and it was from 0.05 mg/kg bw/day to 0.25 mg/kg bw/day (<http://www.efsa.europa.eu/de/efsajournal/pub/2588.htm>). Thus, BHT will constitute between 7% and 15% of the present ADI on daily consumption of a 300 g portion of fish.

5.3.3 Mycotoxins

Plant protein ingredients used in fish feed may contain mycotoxins. A risk assessment on mycotoxins in cereal grain in Norway (VKM, 2013c), however, states that too little data and knowledge exist on this issue for fish health. Information of the transfer of mycotoxins from feed to fillet in Atlantic salmon, is scarce. However, recent available data on deoxynivalenol (DON) and ochratoxin A (OTA) show that the transfer from fish feed to fillet is negligible implying no risk for consumers of the fish (Bernhoft et al., 2014).

5.3.4 Polycyclic aromatic hydrocarbons

Vegetable oils may be contaminated by polycyclic aromatic hydrocarbons (PAHs) due to technological processes such as direct fire drying of grain and oilseeds. Thus vegetable oil are a potential contamination source of PAHs in fish feed (EFSA, 2007; Speer et al., 1990). The PAH levels in vegetable oils for human consumption are reduced by processing techniques (EFSA, 2007) or direct decontamination with the use of active carbon and deodorisation (Larsson et al., 1987). In a research project where 80% of the fish meal and 70% of the fish oil in Atlantic salmon diets was replaced with vegetable ingredients, the diets contained 16-fold more of the most toxic PAH, benzo[a]pyrene (Berntssen et al., 2010a). However, due to high degree of metabolism of PAHs in fish the transfer of PAHs from feed to fillet was so low that the sum of all 16 PAHs in fillet was 25-fold lower than the maximum limit for one of the PAHs, benzo[a]pyrene, in seafood (Berntssen et al., 2010a). Fish feed surveillance revealed a mean concentration of PAH₄ in 2013 at 1.9 µg/kg (Figure 5.3.4-1; (Sanden et al., 2014). Based on the relatively limited number of feed samples analysed the last 4 years showing large variation, no trend is obvious. This is expected since PAHs are components produced during certain processing procedures which will vary between plant ingredients and also between batches of the same type of plant ingredient.

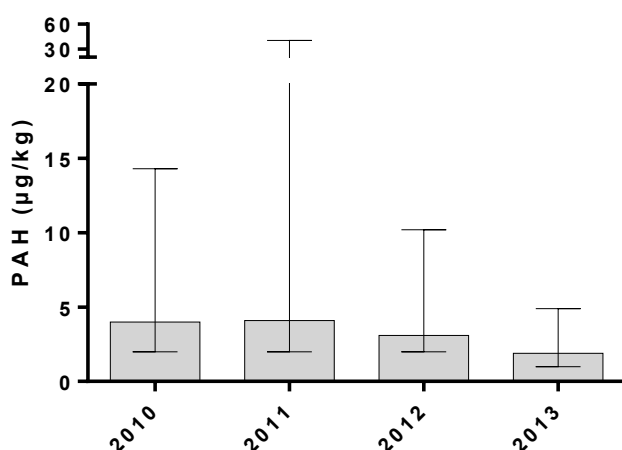


Figure 5.3.4-1 Fish **feed content** of sum polycyclic aromatic hydrocarbons (PAH₄) in the period from 2010 to 2013. Values are upper bound mean with minimum and maximum in µg/kg feed. Upper bound imply that concentrations lower than the limit of detection or limit of quantification is

substituted with the actual value of these limits and not zero, which most likely represent an overestimate of the true values. Numbers of feed samples per year were: n=23 (2010); n=25 (2011); n=23 (2012); n=68 (2013). Source: Sanden et al. (2014)

5.3.5 Brominated flame retardants and perfluorated compounds

In recent years, information has become available about numerous other organic contaminants that may accumulate in the marine food chains. Because these compounds have only recently been identified in marine organisms, however, their potential to transfer from fish feed to fish fillet is not known for all. One group of brominated flame-retardants, seven of the polybrominated diphenyl ethers (PBDE-7), have been monitored for fish feed and farmed Atlantic salmon and trout fillets over the last decade, and trends from the feed surveillance show decreasing concentrations, Figure 5.3.5-1;(Sanden et al., 2014). In 2013, the PBDE-7 content in farmed Atlantic salmon fillet and trout was identical at 0.4 µg/kg (number of samples were 102 and six for Atlantic salmon and trout, respectively).

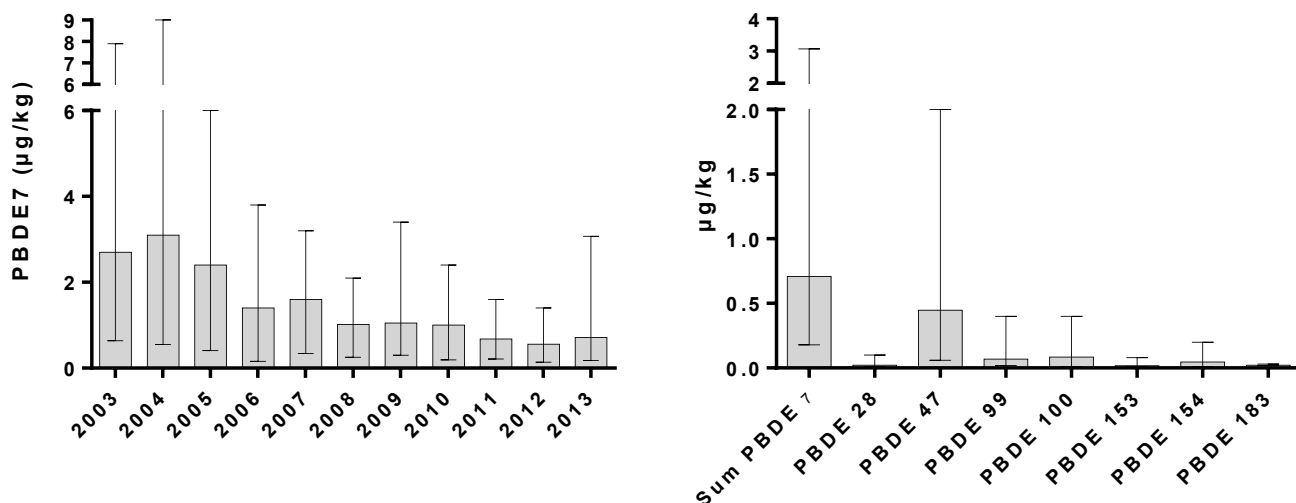


Figure 5.3.5-1 Fish **feed content** of polybrominated diphenyl ethers (PBDE-7) in the period from 2003 to 2013 (left), and the contents of the individual seven PBDE congeners measured in 2013 (right). Values are given as upper bound mean with minimum and maximum levels in µg/kg feed. Upper bound imply that concentrations lower than the limit of detection or limit of quantification is substituted with the actual value of these limits and not zero, which most likely represent an overestimate of the true values. Numbers of feed samples per year were: n=22 (2003); n=10 (2004); n=19 (2005); n=20 (2006); n=22 (2007); n=21 (2008); n=25 (2009); n=23 (2010); n=25 (2011); n=22 (2012); n=69 (2013). Source: Sanden et al. (2014)

The other brominated flame-retardants, hexabromocyclododecan (HBCDs) and tetrabromobisphenol A (TBBPAs), were in 2013 included in the surveillance programs for fish feed, and knowledge on transfer from feed to fish fillet is limited. However, one of the HBCD isomers, HBCDa, was demonstrated to efficiently transfer from fish feed to fish fillet (Berntssen et al., 2011). Model simulations showed HBCDa could range from 0.2 to 1.8

µg/kg fillets with higher levels when the fish oil inclusion was high, and according to the authors of the paper; farmed Atlantic salmon can contribute to a maximum of 6% of the estimated provisional food reference dose for HBCD (Berntssen et al., 2011). The Atlantic salmon surveillance showed that mean fillet total HBCD, of which HBCD_a is the dominating isomer, was 0.4 µg/kg (n=46 samples each of five pooled fish) (Hannisdal et al., 2014). In 2013, Atlantic salmon fillet levels of TBBPA were above the limit of quantification in five of 46 samples. The LOQ ranged from 0.04 to 0.20 µg/kg (Hannisdal et al., 2014).

The perfluorated compounds (18 compounds including PFOS and PFOA) have been included in the monitoring of farmed fish the recent years, and all samples including the 49 sampled in 2013 contained levels below the limit of quantification (LOQ) (Hannisdal et al., 2014). For example for PFOS, the LOQ was between 0.3 and 0.8 µg/kg.

For a range of the compounds there is little data on the levels in fish feed and farmed fish, but if the substances are present in fish feed, it will be important to establish knowledge on their eventual transfer from feed to farmed fish.

5.3.6 Genetically modified plants in fish feed

Through the Agreement of the European Economic Area (EEA), Norway is obliged to implement the EU regulations on genetically modified (GM) food and feed (regulations 1829/2003, 1830/2003). Until implementation of these regulations, Norway has a national legislation concerning processed GM food and feed products that are harmonised with the EU legislation. These national regulations entered into force 15 September 2005. For genetically modified feed and some categories of genetically modified food, no requirements of authorisation were needed before this date. Such products, lawfully placed on the Norwegian market before the GM regulations entered into force, the so-called existing products, could be sold in a transitional period of three years when specific notifications were sent to the Norwegian Food Safety Authority (NFSA). Within three years after 15. September 2005, applications for authorisation had to be sent to the Authority before further marketing.

The Norwegian Seafood Federation (FHL) has once a year since 2008, applied for an exemption of the authorisation requirements of 19 existing GM products. These 19 GM events are all authorised in the EU, and the NFSA has granted exemption for a period of one year at the time.

According to the NFSA, FHL has applied for an exemption in the case of a feed shortage, but no GM ingredients has so far been used by the Norwegian fish feed industry. In October 2014, a new application from the FHL to prolong the exemption was rejected by the NFSA.

The use of GM ingredients in fish feed is surveyed by the NFSA by special surveillance programs. Of the surveilled fish feed samples, none of the abovementioned GM ingredients have been detected.

Due to the limited global supply of marine lipid sources, the inclusion of non-marine plant oils in aqua feeds has increased over the last decades to meet the increased demand from the rapidly expanding production from aquaculture (Nasopoulou and Zabetakis, 2012; Nichols et al., 2014). Further large changes in lipid sourcing are unavoidable if the prognoses for increases in aquaculture production are to be fulfilled (SINTEF, 2013).

Increases in the content of n-3 fatty acids in plant crops can be obtained by traditional breeding. However, genetic modification (GM) is needed for development of plants that can produce long-chain n-3 fatty acids (Opsahl-Ferstad et al., 2003). Some GM varieties of soybean and oilseed rape with modified lipid content and fatty acid profile (lauric (C12), oleic (C16) and linolenic acid (C18 omega-3)) are authorised for food and feed uses (European Chemicals Agency, 2012), but none of these have been modified to produce and accumulate the long-chain n-3 fatty acids. However, transgenic oilseed plants with high-level accumulation of long-chain n-3 fatty acids are under development (Mansour et al., 2014; Miller et al., 2008; Ruiz-Lopez et al., 2014). As such no GM products are yet commercially available, and no scientific information is currently available that can be used for safety assessment of these lipid sources.

Marine protein sources in fish feed can to a large extent be replaced by plant ingredients without genetic modification. Among the protein rich plant ingredients, there are many showing nutritional value that allow inclusion in fish diets at relatively high levels (VKM, 2009). Over the last decade, GM varieties of soybean (80%) and maize have become the dominating varieties on the world market. These raw materials are already replacing non-GM varieties to a large extent in terrestrial animal production.

At present, the GM plant varieties most relevant for fish feeds are derived from soya and maize. Most GM varieties are made resistant against insect or herbicide tolerant by genetic modification. Knowledge on safety of GM feed ingredients in fish diets are accumulating. A thorough review of available relevant fish studies on this issue has been provided by Sissener et al. (2011). The VKM Panel on Genetically Modified Organisms, has in several reports evaluated the safety of the GM feed Event MON810 and considered it, based on current knowledge, to be as safe as non-GM varieties (VKM, 2007; VKM, 2013b).

5.4 Summary of changes in farmed Atlantic salmon feed composition – the significance for nutrients and contaminants in the fillet

The raw materials used in feed for Norwegian farmed Atlantic salmon and trout have substantially changed since 2006. Up to 70% of the fish meal and fish oil are replaced by plant proteins and vegetable oils resulting in some changes in nutrient composition and contaminant composition of fish feed which is reflected in the fish fillet. The changes in feed and the following farmed fish fillet composition since 2006 is;

- Protein (amino acid) composition of farmed fish fillet is not changed.

- Concentrations of EPA+DHA in farmed Atlantic salmon have decreased from ca 3 g/100 g fillet in 2006 to about 1.3 g/100 g in 2013.
- Concentrations of n-6 fatty acids in farmed Atlantic salmon have increased from 1.4 g/100 g in 2005 to ca. 2.3 g/100 g in 2013.
- Since 2006, Atlantic salmon feed concentration of vitamin D₃ has decreased 36% to 0.15 mg vitamin D/kg, concentration of selenium has decreased 45% to 0.15 mg selenium/kg and iodine has decreased 50% to 2.2 mg iodine/kg.
- Concentrations of marine POPs have decreased in fish feed and farmed Atlantic salmon and farmed rainbow trout fillets since 2006. The levels of dioxins and dl-PCBs in 2013 are reduced by almost 70% compared to 2006. In 2013, farmed Atlantic salmon contained 0.5 ng TEQs dioxins and dl-PCBs per kg fillet.
- Mercury has decreased in Atlantic salmon fish feed and fillets due to the increasing fish meal replacement with plant protein sources. Mercury present as methylmercury in farmed Atlantic salmon fillet has decreased 50% since 2006 to 0.014 mg mercury per kg fillet.
- Decontamination of fish oil may further decrease the levels of POPs without affecting the fillet fatty acid levels and composition. Decontamination of fish oil, however, will remove fat-soluble vitamins such as vitamin D.
- The predicted concentrations in fillet following decontamination of fish oil in feed indicate that dioxin and dl-PCBs will be in the same range as in other fatty foods such as cheese (0.29 medium bound WHO-TEQ 2006 ng/kg product) and somewhat higher than beef (0.18 medium bound WHO-TEQ 2006 ng/kg product).
- Fish feed levels of the pesticide endosulfan has been low and stable from 2006 until 2013. In 2013, the level of endosulfan in farmed salmon fillet was low and one dinner serving farmed Atlantic salmon constituted less than 1% of acceptable daily intake.
- New contaminants such as PAH, mycotoxins, and new pesticides are introduced into fish feed when feed ingredients change from marine to plant origin. So far, few studies are available, but those existing indicate that the levels of PAHs and mycotoxins in the feed seem to be low and therefore not expected to represent any risk for food safety. However, more knowledge are needed on the concentrations in fish feed and transfer from feed to fish fillet of new contaminants as well as for the brominated flame retardants and perfluorated compounds.

6 Nutrients and contaminants in fish on the Norwegian market

Data reported in this chapter are based on analytical methods which are accredited in accordance with the standard ISO 17025 (NIFES). The analytical methods for the contaminants and their Limit of Detection (LOD) and Limit of Quantification (LOQ) are described for each set of data reported by Hannisdal et al. (2014), Julshamn and Frantzen (2010), Julshamn et al. (2010), Julshamn et al. (2013d), Nilsen et al. (2010), Nilsen et al. (2012), Nilsen et al. (2013a), Duinker et al. (2013), Frantzen et al. (2009) and Frantzen et al. (2010). The limit of detection (LOD) is the lowest level at which the method is able to detect the substance, while the limit of quantification (LOQ) is the lowest level for a reliable quantitative measurement.

For the calculations of nutrient intake presented in Chapter 7, choices have been made regarding which fish/fish products to include in the calculations of nutrient intake and of which contaminant exposure to use for the various fish/fish products (Chapter 6, Appendix VII). Based on the reported fish consumed in one or several of the surveys (Chapter 3), data on nutrient and contaminant content had both to be available, and representative for fish on the Norwegian market. The concentrations and the rationale for fish species/fish products used for nutrient and contaminant intake and exposure calculations can be found in Appendix VII.

6.1 Content of nutrients in fish and fish products

For further details of sampling, methods for chemical analyses and quality assurance of nutrients and contaminants in fish, see Appendix VI.

6.1.1 Wild and farmed fish species

The content of selected nutrients presented in Table 6.1.1-1 is divided into categories of lean and medium fat fish species, fatty fish species, and fish products. Generally, data available on nutrient composition of wild and farmed fish is limited and based on a relatively low numbers of fish. In contrast to contaminants in wild and farmed fish, which have been either yearly surveilled or included in large baseline studies (as described in Appendix VI), similar major efforts have not yet been done to characterise the nutrient composition in wild and farmed fish. For some wild fish species data are lacking (e.g. redfish and haddock) or most recent data available are analysed in 2005. The data from 2005 are still included in this report since variation in wild fish nutrients is not expected to change significantly over time. This is in contrast to farmed fish, where the diet composition have changed since the 2006 report having consequences for the composition of several of the nutrients in farmed fish fillet. The time-trends for farmed Atlantic salmon are presented in Chapter 5 in this report.

6.1.1.1 Fat content

In the category lean and medium fatty fish, the mean total fat content range from 0.6 g per 100 g in haddock to 2.8 g per 100 g in redfish. In the fatty fish category total fat content ranges from 7.6 g per 100 g in farmed halibut to 32.1 g per 100 g in mackerel. Wild halibut was analysed in 2005 for nutrients, and although the size of halibuts analysed included small and large specimens (as described in Appendix VI) mean total fat content was analysed to be only 2.3 g per 100 g. This low total fat content is likely due to only the lean part of the fillet being analysed, which is the part of the halibut that normally is consumed whereas the fattier outer part is cut away. In spite of the analysed value of total fat in wild halibut is within the range of lean and medium fat fish, halibut is normally categorised as fatty fish and hence also here included as fatty fish. The halibut analysed for nutrients were not the same fish samples described for analyses of contaminants.

6.1.1.2 Fatty acid content

The highest level of sum EPA+DPA+DHA was found in mackerel and the lowest in Greenland halibut. DPA typically contributes with 20%, of sum EPA+DPA+DHA, whereas EPA+DHA contribute with the remaining 80%. Sum n-3 is always higher than sum EPA+DPA+DHA since additional n-3 fatty acids are included in sum n-3. These are 16:3n-3, 16:4n-3, 18:3n-3, 18:4n-3, 20:3n-3, 20:4n-3, 24:5n-3 and 24:6n-3. Generally, the difference between sum EPA+DPA+DHA and sum n-3 is higher in the fattier fish species than the lean fish species. For example, the fattiest species mackerel had 1.5 fold higher sum n-3 than sum EPA+DPA+DHA whereas Atlantic cod fillet had hardly any increase in sum n-3 compared to sum EPA+DPA+DHA. In fish, most of EPA, DPA and DHA are membrane bound structural lipids. Surplus EPA+DPA+DHA and other n-3 fatty acids are mainly stored in body fat as triacylglycerols (TAGs) resulting in a higher sum n-3. Cod has negligible TAG stores in muscle, whereas fatty fish can have substantial TAG levels as fat stores in the fillet. This is reflected in the similar EPA+DPA+DHA and sum n-3 in lean fish fillet (e.g. cod), whereas sum n-3 is higher than EPA+DPA+DHA in fatty fish fillets (e.g. mackerel).

Farmed Atlantic salmon has almost twice the sum of n-3 PUFA compared to sum EPA+DPA+DHA, and 18:3n-3 (linolenic acid) from vegetable oil is the main fatty acid contributing to the higher sum of n-3. Compared to 2006, sum EPA+DPA+DHA in fish fillets has decreased by 50% whereas sum n-3 has decreased by 30%. The lower decrease in sum n-3 is due to the increase in 18:3n-3 (linolenic acid, mainly from rapeseed oil) in farmed salmon fillet in 2013 compared to the 2006 report.

Sum of n-6 PUFA is included in Table 6.1-1 to document the increase in n-6 PUFA when fish oil is replaced by vegetable oils. In the wild fish species, sum of n-3 PUFA is typically 10 fold higher than sum of n-6 PUFA. In farmed Atlantic salmon in 2013, sum of n-3 PUFA is approximately equal to sum of n-6.

In the 2006 VKM report, farmed Atlantic salmon was reported to contain 520 mg n-6 PUFA per 100 g, 3200 mg n-3 PUFA per 100 g, and 2700 mg EPA+DPA+DHA per 100 g, thus containing six times more sum n-3 PUFA than sum n-6 PUFA.

The fatty acids included in the sum n-6 PUFA are 18:2n-6, 18:3n-6, 20:2n-6, 20:3n-6, 20:4n-6, 22:4n-6 and 22:5n-6. Of the sum n-6 PUFA, 18:2n-6 (linoleic acid) is the dominating fatty acid in farmed Atlantic salmon, whereas the long-chain 20:4n-6 (arachidonic acid) accounts for a higher relative portion of sum n-6 PUFA in wild fish species.

6.1.1.3 Vitamin D

The content of vitamin D (as D₃) is naturally highest in the fatty fish species. Also within the fatty fish species, the content of vitamin D varies independently of fillet lipid content. Herring contain the highest vitamin D at 14.5 µg/100 g whereas mackerel has the lowest vitamin D content at 2.8 µg per 100 g. This is in contrast to mackerel containing 2-fold more fat per 100 g compared to herring.

In the 2006 VKM report, farmed Atlantic salmon contained 8 µg vitamin D/100 g. The current vitamin D concentration (analysed as D₃) in farmed Atlantic salmon is reported to be similar (7.5 µg/100 g) compared to 2006.

6.1.1.4 Selenium and iodine

Selenium fillet concentrations were all within a relatively narrow range in the wild fish species varying from 24 µg/100 g in cod to 58 µg/100 g in herring. Farmed Atlantic salmon contained 12 µg/100 g in 2013, as also described and discussed in Chapter 5.

Lean marine fish, such as Atlantic cod and saithe, contain the highest levels of iodine being 100-fold higher compared to the fatty fish species.

Data on nutrients in freshwater fish is scarce and mainly lacking.

In the 2006 VKM report, farmed Atlantic salmon contained 30 µg selenium per 100 g and 6-34 µg iodine per 100 g. Today's farmed Atlantic salmon contains less selenium (12 µg per 100 g) and iodine (4 µg per 100 g) than the corresponding levels in 2006.

6.1.1.5 Sandwich spreads

The sandwich spreads based on liver from codfish were typically high in fat, EPA+DPA+DHA, vitamin D, iodine and selenium. All these nutrients were present in higher concentrations in the cod liver compared to in fillets of wild and farmed fish species. The ratio between sum n-3 and sum n-6 were approximately 10 to 1 as it were for all the wild fish species. For concentrations of n-3 fatty acids, vitamin D, iodine and selenium used in the intake assessment in Chapter 7, see Appendix VII.

Table 6.1.1-1 Concentration of nutrients in lean and fatty fish and fish products given as mean per 100 grams fish fillet/edible product

Food item	n	Year	Fat g/100g Mean (SD)	Sum EPA+DPA+DHA mg/100g Mean (SD)	Sum n-3 mg/100g Mean (SD)	Sum n-6 mg/100g Mean (SD)	Vitamin D µg/100g Mean (SD)	Iodine µg/100g Mean (SD)	Selenium µg/100g Mean (SD)
Lean fish (≤ 5% fat)^a									
Atlantic cod ^b	51	2006/07/11	1.1 (0.1)	273 (53)	282 (53)	22 (4)	<1	323 (425)	24 (3)
Saithe ^c	40	2006/11	1.4 (0.6)	439 (191)	458 (199)	27 (11)	1.4 (0.2)	160 (95)	30 (14)
Haddock ^d	-	No data	0.6	No data	No data	No data	0.7	No data	28
Plaice	15-20	2007	2.6 (1.0)	623 (271)	709 (308)	74 (29)	6.5 (8.2)	14 (3)	34 (7)
Redfish ^d	-	-	2.8	No data	No data	No data	No data	No data	50
Wolffish ^e	3	2011	0.9 (0.5-1.1)	223 (137-325)	250 (149-346)	121 (89-175)	<0.1	124 (114-133)	29 (25-31)
Tuna, canned ^d	-	-	1	No data	No data	No data	1.6	8	200
Fatty fish (>5% fat)^a									
Atlantic halibut ^f	53	2005	2.3 (2.0)	612 (410)	709 (502)	80 (58)	12 (8.2)	18 (10)	No data
Farmed Atlantic halibut	15	2005	7.6 (2.3)	1450 (399)	1822 (516)	389 (126)	8.5 (3.1)	No data	28 (8)
Greenland halibut ^g	18	2006/11	13 (2.0)	1053(141)	1358 (91)	258 (36)	12 (0.2)	10 (2)	50 (16)
Herring (Norwegian spring spawning) ^h	30	2005/10	9.9 (5.0)	1655 (1130)	2213 (1637)	170 (90)	15 (9.2)	2 (1)	58 (8)
Herring (North Sea) ⁱ	44	2005/06/10	14 (2.1)	2479 (388)	3543 (666)	375 (123)	7.7 (1.7)	12 (3)	50 (8)
Mackerel (North Sea)	10	2006	32 (1.4)	6471 (498)	9568 (751)	755 (59)	4.4 (1.4)	No data	49 (3)
Mackerel (North East Atlantic)	10	2010	23 (3.7)	4456 (629)	6738 (1045)	605 (105)	2.8 (0.8)	17 (3)	52 (4)
Wild Atlantic salmon (Sørfjorden)	27	2012	8.7 (2.8)	2016 (363)	2485 (520)	268 (61)	11 (5.3)	14 (6)	46 (8)
Wild Atlantic salmon (Finnmark)	99	2012	8.0 (2.7)	1765 (515)	2126 (650)	193 (72)	No data	No data	44 (15)
Farmed Atlantic salmon ^j	90	2013	15 (2.2)	1311 (166)	2303 (285)	2296 (377)	7.5 (2.6)	4 (2)	12 (3)
Farmed Atlantic salmon ^k	100	2012	14 (2.7)	1590 (345)	2582 (494)	2149 (557)	6.3 (3.0)	2 (1)	14 (3)
Freshwater fish									
Perch ^d	-	-	1.3	No data	No data	No data	0.8	18	28
Brown trout	-	-	No data	No data	No data	No data	No data	No data	No data
Pike ^d	-	-	0.7	No data	No data	No data	0.9	20	22
Sandwich spreads from fish									
Cod roe and liver pate ^d	-	2014	39	No data	No data	No data	39	234	60
Cod roe and liver pate ^l	-	-	33	5500 (EPA+DHA)	6600	No data	No data	No data	No data
Mackerel in tomato sauce ^d	-	2014	19	No data	No data	No data	2.9	No data	30

Food item	n	Year	Fat g/100g Mean (SD)	Sum EPA+DPA+DHA mg/100g Mean (SD)	Sum n-3 mg/100g Mean (SD)	Sum n-6 mg/100g Mean (SD)	Vitamin D µg/100g Mean (SD)	Iodine µg/100g Mean (SD)	Selenium µg/100g Mean (SD)
Mackerel in tomato sauce ^e	7	2006	19 (11-27)	2731 (1319-5235) (EPA+DHA)	4238 (1911- 8073)	1886 (888-2557)	4.3 (2.3-8.4)	No data	30 (20-40)
Caviar (based on cod roe) ^d	-	2014	35	No data	No data	No data	0	85	41
Cod roe									
Atlantic cod roe ^l	5	2014	6.4	300 (EPA+DHA)	700	No data	No data	No data	No data
Atlantic cod roe ^d	-	2014	2.7	No data	No data	No data	12	104	9.0
Fish liver									
Saithe liver ^m	30	2006	76 (2.6)	15402 (349)	18417 (838)	1796 (639)	120 (30)	144 (20)	82 (6)
Atlantic cod liver ⁿ	41	2006/07	59 (4.3)	11296 (655)	13477 (731)	1323 (34)	89 (24)	379 (186)	80 (3)
Cod liver for use in cod roe and liver pâté ^l	6	2014	61	13050 (EPA + DHA)	14570	176	No data	No data	No data

^aLean fish is fish with fat content below 2%, medium fatty fish have 2-5% fat, and fatty fish have more than 5% fat. Halibut is categorised as fatty fish in this opinion, ^bMean of cod harvested in the Norwegian Sea 2006 (10 samples), North Sea 2011 (10 samples) and Barents Sea 2006 (20 samples) and 2007 (11 samples). For vitamin D, 42 samples were analysed, ^cMean of saithe harvested in the North Sea 2006, Barents Sea 2006 and 2011, Haltenbank 2006 (10 samples per harvesting), ^dValues according to the Norwegian Food Composition Table, 2014, ^eDue to few samples, SD is not given but minimum and maximum values, ^fMean of 53 samples of halibut harvested in Norwegian Sea and North Sea in 2005, ^gMean of Greenland halibut harvested in Barents Sea 2006 (8 samples) and 2011 (10 samples). For iodine, 10 samples were analysed, ^hMean of Norwegian Spring Prawning herring from the Norwegian Sea 2005 and 2010, and the North Sea 2005 (10 samples per harvest). For iodine, 10 samples were analysed, ⁱMean of North Sea herring harvested in the North Sea 2005 (9 samples), 2006 (10 samples) and 2010 (25 samples), ^jMean of 90 samples of farmed salmon harvested in 2013, except for analysis of vitamin D where 70 samples were analysed, ^kMean of 100 samples of farmed salmon harvested in 2012, except for analysis of vitamin D where 69 samples were analysed, ^lValues from the food industry, 2014. Samples of cod liver for use in cod roe/liver pâté were pooled samples taken from six whole cans, ^mFor iodine, nine samples were analysed, and for selenium, 71 samples were analysed, ⁿMean content in cod liver from cods harvested in the Barents Sea in 2006 (21 samples) and 2007 (10 samples) and in the Norwegian Sea in 2006 (10 samples).

6.1.2 Fish oil and/or cod liver oil

Only eight cod liver oil samples were analysed for nutrient composition from 2007 to 2010 (Table 6.1.2-1). Of these the EPA+DPA+DHA content was naturally high with 5 ml of oil contributing with approximately 1.4 g EPA+DPA+DHA. Vitamin D content was expected to be approximately 200 µg per 100 g based on the labelling of cod liver oil (10 µg per 5 ml). The mean vitamin D content was analysed to be 233 µg per 100 g, and the 95th percentile were 105 µg per 100 g. Hence, the mean vitamin D content was within the range that can be expected in cod liver oil.

Table 6.1.2-1 Nutrients in cod liver oils and n-3 oil based food supplements of the Norwegian market given as mean with minimum and maximum values in parentheses

Supplement	Year	n	Fat %	Sum EPA+DHA+DPA mg/100g	Sum n-3 mg/100g	Vitamin D µg/100g
Cod liver oil	2007-2010	8	100	28400 (18400-49300)	32800 (21700-53100)	233 (53-300)
Fish oils	2007-2011	13	100	28100 (12594-82600)	34500 (19500-69200)	73 (<1-460)

Source: NIFES (unpublished data)

Fish oils are a heterogeneous group with no standard regarding vitamin D content. It is therefore as expected that the vitamin D content varies widely (from not detected to 460 µg per 100 g) whereas the sum n-3 and sum EPA+DPA+DHA was at comparable concentrations as cod liver oil.

6.2 Contaminants in fish and fish products

6.2.1 Wild and farmed fish species and fish products

6.2.1.1 Concentration of mercury in fish

The available data on contaminant concentrations in wild and farmed fish, and fish products have been expanded substantially since 2006 due to yearly surveillance of farmed fish and several large base line studies of the commercially relevant wild fish species. The data used in this report is thus considered representative for the vast majority of species (Table 6.2.1.1-1). There are some exceptions, such as wolffish (n=10 from 2003 and n=25 from 2005), haddock (n=25), tuna (n=6) and sprat (n=14) with low number of fish being analysed and where most recent data are from before 2006. However, for the species being most relevant for consumption in Norway, which is the target for this report, data are available from large base line studies and/or national and/or EU surveillance programs (Appendix VI).

As expected, the large wild fish species such as halibut, Greenland halibut and tuna have the highest mercury fillet concentrations of the marine fish species. Fresh water species

contained even higher concentrations than the marine fish, and pike contained the highest mercury concentrations at 0.57 mg per kg (Table 6.2.1.1-1). The lowest mercury concentrations were found in farmed Atlantic salmon in 2012 and 2013 at 0.014 mg per kg fillet. This was expected based on the feed ingredients used (Chapter 5) combined with fast growth and relatively short production time in modern farming of Atlantic salmon. In the 2006 VKM report, farmed Atlantic salmon were reported to contain 0.030 mg mercury /kg fillet (w.w.).

In fish fillets the majority of mercury is present as methylmercury. As an example farmed Atlantic salmon and rainbow trout were analysed for methylmercury and mercury, and data show that all the mercury was present as methylmercury. Therefore, as a conservative approach in this report all total mercury data in fish is considered as methylmercury.

Except for "cod roe and liver pate" (in Norwegian: Svolværpostei) which was analysed to have mercury levels below LOQ, mercury was present in quantifiable levels (above LOQ) in all fish species. This is also evident by the upper bound (UB) and lower bound (LB) levels being the same or very similar in all fish species analysed.

Cod liver oil and fish oil contained very low mercury levels compared to fillets of wild and farmed fish (Table 6.2.1.1-2), down towards, or at, the limit of quantification.

For details of sampling, methods for chemical analyses and quality assurance of contaminants in fish, see Appendix VI. For mercury concentrations used in the exposure assessment in Chapter 7, see Appendix VII.

Table 6.2.1.1-1 Concentration of mercury (Hg) in fish and fish products. Upper and lower mean levels with minimum and maximum values in parenthesis.

Fish species/fish product	Sampling year	n	Mean mg Hg/kg fillet (wet weight) (min.-max.)		LOQ mg Hg/kg fillet (ww)
			Lower bound	Upper bound	
Lean fish ($\leq 5\%$ fat)^a					
Cod, all populations	2009-2011	2109	0.075 (0.004-0.70)	0.075 (0.004-0.70)	0.001
Cod (coastal)	2010-2011	687	0.11 (0.012-0.71)	0.11 (0.012-0.71)	0.001
Cod (North Sea)	2010-2011	516	0.11 (0.004-0.54)	0.11 (0.004-0.54)	0.001
Cod (North East Atlantic)	2009-2010	906	0.035 (0.006-0.17)	0.035 (0.006-0.17)	0.001
Saithe	2010-2012	1620	0.051 (0.01-0.66)	0.051 (0.01-0.66)	0.001-0.002
	2006-2013	124	0.051 (0-0.21)	0.051 (0.007-0.21)	0.001-0.008
Haddock	2003	25	0.08 (0.04-0.12)	0.08 (0.04-0.12)	Not given
Plaice	2007	156	0.070 (0.009-0.40)	0.070 (0.009-0.40)	0.004-0.008
Redfish	2007	178	0.13 (0.011-1.1)	0.13 (0.011-1.1)	0.005-0.009
Wolffish	2003	10	0.021 (0-0.18)	0.025 (0.006-0.18)	0.006
	2005	25	No data	0.11 (0.056-0.15)	Not given
Tuna, canned	2006	6	0.10 (0.035-0.20)	0.10 (0.035-0.20)	0.008
Fatty fish ($>5\%$ fat)^a					
Atlantic halibut ^b	2006-2010	88	0.26 (0.020-1.2)	0.26 (0.020-1.2)	0.001-0.02
B-section		40	0.29 (0.020-1.2)	0.29 (0.020-1.2)	0.001-0.02
I- section		39	0.21 (0.020-0.77)	0.29 (0.020-1.2)	0.001-0.02
B+I- section		79	0.25 (0.020-1.2)	0.25 (0.020-1.2)	0.001-0.02
Greenland halibut	2006-2008	1288	0.22 (0.009-1.2)	0.22 (0.009-1.2)	0.003-0.01
Herring (Norwegian spring spawning)	2006-2007	800	0.039 (0.008-0.40)	0.039 (0.008-0.40)	0.006-0.015
Herring (North Sea)	2009-2010	862	0.050 (0.010-0.23)	0.050 (0.010-0.23)	0.001-0.003
Mackerel (North East Atlantic)	2007-2009	845	0.039 (0-0.36)	0.039 (0.009-0.36)	0.009-0.03
Sprat ^c	2010	14	0.019 (0.009-0.027)	0.019 (0.009-0.027)	0.005
Wild Atlantic salmon	2012	98	0.036 (0.014-0.13)	0.036 (0.014-0.13)	0.001-0.002
Farmed Atlantic salmon ^d	2013	132	0.014 (0.007-0.041)	0.014 (0.007-0.041)	0.002
	2012	305	0.014 (0.007-0.042)	0.014 (0.007-0.042)	Not given
Farmed trout ^d	2013	20	0.018 (0.011-0.053)	0.018 (0.011-0.053)	0.002

Fish species/fish product	Sampling year	n	Mean mg Hg/kg fillet (wet weight) (min.-max.)		LOQ mg Hg/kg fillet (ww)
			Lower bound	Upper bound	
	2010	155	No data	0.02 (0.01-0.04)	Not given
Farmed Arctic char	2010	25	No data	0.03 (0.02-0.04)	Not given
Freshwater fish^e					
Perch	1965-2008	>5000	0.33 (0.01-4.2)	0.33 (0.01-4.2)	Not given
Brown trout	1965-2008	>2500	0.12 (0.01-3.1)	0.12 (0.01-3.1)	Not given
Pike	1965-2008	24520	0.57 (0.01-6.0)	0.57 (0.01-6.0)	Not given
Sandwich spreads from fish					
Cod roe and liver pate ^f	2008	2	<0.02	<0.02	0.02
Cod roe and liver pate ^g	2014	7	<0.011	<0.011	0.005 -0.011
Cod roe ^g	2014	-	Not detected	Not detected	0.005 -0.011
Fish liver					
Cod liver, all populations	2009-2011	1908	0.042 (0.00-1.6)	0.045 (0.004-1.6)	0.004-0.03
Cod (coastal)	2010-2011	638	0.073 (0.00-1.6)	0.074 (0.004-1.6)	0.005-0.03
Cod (North Sea)	2010-2011	434	0.051 (0.00-0.21)	0.051 (0.01-0.21)	0.01-0.03
Cod (North East Atlantic)	2009-2010	836	0.014 (0.00-0.12)	0.019 (0.004-0.12)	0.004-0.02
Saithe liver	2010-2012	1590	0.013 (0.0-0.42)	0.015 (0.002-0.421)	0.002-0.03

^aLean fish is fish with fat content below 2%, medium fatty fish is fish with 2-5% fat, and fatty fish is fish with >5% fat. Halibut is categorised as fatty fish in this opinion.

^bFor halibute, see Appendix VII for definition of B and I sections, ^cWhole, freshly caught sprat were analysed, ^dFor farmed salmon and trout, pooled samples of five fish each were analysed, ^eValues for fresh water fish are from Jenssen et al. (2012), ^fTwo pooled samples of five cans each based on ten samples from different batches. Each can consisted of 40% cod roe, 24% cod liver, soy oil, cod liver oil, vinegar, tomato puree and water (Julshamn and Frantzen (2009); Julshamn and Frantzen (2010)), ^gData from the food industry.

Table 6.2.1.1-2 Concentrations of mercury in cod liver oil and n-3 oil based food supplements on the Norwegian market.

Supplement	Year	n	Lower bound mg/kg	Upper bound mg/kg	Level of quantification (LOQ) mg/kg
Cod liver oil ^a	2010-2013	6	<0.005	0.004 (0.003-0.005)	0.003-0.005
Fish oils ^a	2009-2013	33	<0.003-0.029	0.009 (0.003-0.029)	0.003-0.029

^aData from (Julshamn and Frantzen (2009); Julshamn and Frantzen (2010))

6.2.1.2 Dioxins and PCBs

The available data on contaminant concentrations in wild and farmed fish and fish products have been expanded substantially since 2006 due to yearly surveillance of farmed fish and several large base line studies of the commercially relevant wild fish species. However, as described in Appendix VI, analyses of dioxins and dl-PCBs were done for a limited number of samples of lean fish fillet such as Atlantic cod (n=136) and a high number of lean fish livers such as Atlantic cod livers (n=2050).

The majority of analyses have been performed after the 2006 report, and hence updated and solid data sets are available for the vast majority of relevant fish species for human consumption.

As expected, the lean fish fillets contained several fold lower concentrations of dioxins and dl-PCBs compared to the medium fatty and fatty fish fillets. Livers and roe from Atlantic cod contained the highest concentrations at more than 21 ng 2005-TE dioxins and dl-PCBs (Table 6.3-1). Of the fatty wild fish species halibut, both Greenland- and Atlantic halibut, contained the highest concentrations at 4.4 ng 2005-TE per kg fillet, whereas NVG herring had the lowest concentrations at 0.63 ng 2005-TE per kg fillet. Farmed Atlantic salmon fillets containing 0.5 ng 2005-TE dioxins and dl-PCBs per kg fillet (Table 6.2.1.2-1) had lower concentrations than all the wild fatty fish species. In the 2006 VKM report, farmed Atlantic salmon were reported to contain 1.7 ng dioxins and dl-PCBs TEQ/kg, 1.2 ng dl-PCBs TEQ/kg, and 0.5 ng dioxins TEQ/kg. Hence, the content of dioxins and dl-PCBs were more than tree-fold higher in 2006 compared to todays farmed Atlantic salmon.

Concentration of dioxins and dl-PCBs in cod liver oil and fish oil (Table 6.2.1.-2) ranged from 0.59 to 1.1 ng 2005-TE per kg based on upper bound (UB) values. It is, however, important to note that the difference between LB and UB concentrations was from 2 to 5 fold, indicating that a high proportion of the UB concentration was due to using LOQ of different congeners.

For further details of sampling, methods for chemical analyses and quality assurance of contaminants in fish, see Appendix VI. For concentrations of dioxin and dl-PCBs used in the exposure assessment in Chapter 7, see Appendix VII.

Table 6.2.1.2-1 Sum dioxins and dioxin-like PCBs given as mean nanogram (ng) 2005-TE/kg wet weight (ww) fish fillet and fish products. Upper and lower mean levels with minimum and maximum values in parenthesis.

Food item	Year	n	Mean sum dioxins and dl-PCBs ng TEQ/kg ww		Mean dioxins ^a ng TEQ/kg ww		Mean dl-PCBs ^b ng TEQ/kg ww	
			Lower bound	Upper bound	Lower bound	Upper bound	Lower bound	Upper bound
Lean fish (≤ 5% fat)^c								
Atlantic cod	2007-2010	136	0.035 (0.0049-0.12)	0.056 (0.0057-0.16)	0.005 (0-0.042)	0.025 (0.0024-0.14)	0.030 (0.0016-0.12)	0.030 (0.0026-0.12)
Saithe	2006	41	0.072 (0.031-0.14)	0.097 (0.054-0.16)	0.005 (0-0.033)	0.029 (0.020-0.082)	0.067 (0.029-0.13)	0.067 (0.029-0.13)
Haddock	2003	7	0.045 (0.026-0.069)	0.054 (0.030-0.091)	0.010 (0.004-0.017)	0.020 (0.013-0.028)	0.034 (0.017-0.063)	0.034 (0.017-0.064)
Plaice	2007	25	0.33 (0.12-1.4)	0.34 (0.14-1.4)	0.098 (0.025-0.35)	0.11 (0.045-0.36)	0.23 (0.088-1.0)	0.23 (0.088-1.0)
Redfish	2004	24	0.60 (0.18-2.0)	0.61 (0.19-2.2)	0.20 (0.052-0.35)	0.22 (0.060-0.53)	0.39 (0.12-1.6)	0.39 (0.12-1.6)
Wolffish	2003	10	0.49 (0.046-2.6)	0.49 (0.051-2.6)	0.23 (0.013-1.3)	0.23 (0.016-1.3)	0.26 (0.024-1.3)	0.26 (0.024-0.3)
Tuna, canned	-	-	No data	No data	No data	No data	No data	No data
Fatty fish (>5% fat)^c								
Atlantic halibute	2006-2010	90	4.0 (0.068-48)	4.4 (0.10-48)	1.1 (0.010-11)	1.1 (0.036-11)	3.3 (0.052-39)	3.3 (0.052-39)
Greenland halibute	2006-2008	1028	4.3 (0.37-17)	4.4 (0.38-17)	1.7 (0.09-9.3)	1.7 (0.09-9.3)	2.6 (0.28-9.7)	2.6 (0.29-9.7)
Herring (Norwegian spring spawning)	2006-2007	799	0.56 (0.14-2.7)	0.63 (0.21 -2.9)	0.28 (0.061-1.8)	0.32 (0.11-1.9)	0.28 (0.077-0.90)	0.31 (0.086-0.99)
Herring (North Sea)	2009-2010	875	1.0 (0.13-5.2)	1.2 (0.27-5.4)	0.52 (0.064-2.9)	0.72 (0.16-3.9)	0.48 (0.053-2.3)	0.53 (0.06-2.5)
Mackerel (North East Atlantic)	2007-2009	785	0.63 (0.019-9.4)	0.87 (0.12-9.7)	0.14 (0-2.8)	0.37 (0.054-3.1)	0.49 (0.013-6.5)	0.49 (0.036-6.8)
Sprat ^d	2010	14	1.1 (0.22-2.4)	1.3 (0.40-2.4)	0.49 (0.10-1.1)	0.66 (0.21-1.2)	0.64 (0.12-1.2)	0.64 (0.12-1.2)
Wild Atlantic salmon	2012	92	0.82 (0.29-1.50)	0.96 (0.36-2.04)	0.28 (0.07-0.58)	0.42 (0.13-1.69)	0.54 (0.23-0.95)	0.54 (0.227-0.95)
Farmed Atlantic salmon	2013	102	0.36 (0.02- 1.49)	0.52 (0.18-1.5)	0.08 (0.00-0.54)	0.24 (0.12-0.56)	0.28 (0.02-0.94)	0.28 (0.026-0.94)
Farmed trout	2013	6	0.33 (0.17-0.52)	0.58 (0.30-0.86)	0.06 (0.04-0.07)	0.31 (0.17-0.42)	0.27 (0.12-0.46)	0.27 (0.12-0.46)
Freshwater fish								
Perch	-	-	No data	No data	No data	No data	No data	No data
Brown trout	-	-	No data	No data	No data	No data	No data	No data
Pike	-	-	No data	No data	No data	No data	No data	No data
Sandwich spreads from fish								
Cod roe and liver pate ^e	2008	2	2.3-3.7	2.3-3.8	0.38-0.53	0.46-0.63	1.9-3.1	1.9-3.1
Cod roe and liver pate ^f	2010-2014	7	No data	4.43 (3.5- 5.0)	No data	0.61 (0.56-0.75)	No data	3.82 (2.9-4.39)
Mackerel in tomato sauce ^g	2001-2005	4	0.75	No data	0.22	No data	0.53	No data

Food item	Year	n	Mean sum dioxins and dl-PCBs ng TEQ/kg ww		Mean dioxins ^a ng TEQ/kg ww		Mean dl-PCBs ^b ng TEQ/kg ww	
			Lower bound	Upper bound	Lower bound	Upper bound	Lower bound	Upper bound
Cod roe ^g	2005	4	0.32	No data	No data	0.074	0.25	No data
Cod liver ^h	2009-2011	2050 ^{h1}	No data	21.3 (1.0-276)	No data	4.7 (0.27-86)	No data	167 (0.49-263)
	2009-2011	528 ^{h2}	21 (1.7-175)	22 (2.4-176)	0.98 (0.18-24)	4.8 (0.96-26)	16.9 (1.4-168)	17 (1.4-168)

^a Dioxin = PCDD/F - polychlorinated dibenzo-para-dioxins (PCDD) and polychlorinated dibenzo furans (PCDF), ^bdl-PCBs = dioxin-like PCB (non-ortho and mono-ortho substituted PCBs), ^cLean fish has fat content below 2%, medium fatty 2-5% fat and fatty fish more than 5% fat. Halibut is categorised as fatty fish in this opinion, ^dWhole, freshly caught sprat were analysed, ^eTwo pooled samples of five cans each based on ten samples from different batches. Each can consisted of 40% cod roe, 24% cod liver, soy oil, cod liver oil, vinegar, tomato puree and water (Julshamn and Frantzen (2009); Julshamn and Frantzen (2010)), ^fData from the food industry: one pooled samples in 2010, 2013, 2014 and two in 2011 and 2012, respectively, ^gData from Kvaalem et al. (2009), ^hData from (Julshamn and Frantzen (2009); Julshamn and Frantzen (2010)) ^{h1}All cod liver samples, ^{h2}Data based on a subset of the samples with given LOQ.

Table 6.2.1.2-2 Sum dioxins and dioxin-like PCBs given as mean nanogram (ng) 2005-TEQ/kg cod liver oil and fish oil. Upper and lower mean levels with minimum and maximum values in parenthesis.

Supplement	Year	n	Mean sum dioxins and dl-PCBs ng 2005-TEQ/kg ww		Mean dioxins ^a ng TEQ/kg ww		Mean dl-PCBs ^b ng TEQ/kg ww	
			Lower	Upper	Lower	Upper	Lower	Upper
Cod liver oil ^c	2012-2014	8	0.10 (0.036-0.19)	0.59 (0.51-0.74)	Not detected	0.33 (0.29-0.36)	0.10 (0.036-0.19)	0.27 (0.21-0.40)
Cod liver oil ^d	2006, 2010-2013	12	No data	1.1 (0.47-2.1)	No data	0.48 (0.24-1.2)	No data	0.66 (0.18-1.8)
	2011-2013	5	0.46 (0.17-1.1)	1.1 (0.47-2.1)	0.17 (0-0.24)	0.74 (0.29-1.2)	0.30 (0.0002-0.86)	0.39 (0.18-0.87)
Fish oils ^d	2006, 2008-2013	51	No data	1.1 (0.19-9.2)	No data	0.65 (0.16-1.7)	No data	0.43 (0.016-7.5)
	2011-2013	14	0.29 (0.008-0.93)	1.1 (0.19-2.0)	0.16 (0.0-0.44)	0.86 (0.16-1.5)	0.13 (0-0.49)	0.22 (0.034-0.56)

^a Dioxin = PCDD/F - polychlorinated dibenzo-para-dioxins (PCDD) and polychlorinated dibenzo furans (PCDF), ^bdl-PCBs = dioxin-like PCB (non-ortho and mono-ortho substituted PCBs), ^cInformation from food industry in Norway: Eight pooled samples based on 97 individual samples LOQ 0.11 for sum PCDD/F + dl-PCBs, 0.07 for PCDD/F, and 0.04 for dl-PCBs. The methods uncertainty is 16%, ^dData from (Julshamn and Frantzen (2009); Julshamn and Frantzen (2010))

6.3 Summary of nutrients and contaminants in fish on the Norwegian market

- The available data on nutrient concentrations in wild fish and fish products have expanded since 2006, but data is still lacking for some nutrients, and number of fish analysed is still very limited for several of the species. For some wild fish species, data are lacking, or the most recent data available are analysed in 2005. Compared to VKM (2006), the overall conclusions in 2014 are that there are few changes in composition and concentrations of nutrients in wild caught fish.
- The available data on contaminant concentrations in wild and farmed fish and fish products have expanded substantially since 2006 due to several large base line studies of the commercially relevant wild fish species and yearly surveillance of farmed fish. Taking into consideration the scarce data available in 2006, there are minor or no changes in levels of mercury and sum dioxins and dl-PCBs in wild fish species since 2006. The exception is sum dioxins and dl-PCBs in herring, where data in the 2006 report showed 1.9 ng/kg, which has decreased to 0.63 ng TEQ/kg in 2014.
- Nutrient and contaminant concentration data in farmed Atlantic salmon is the most recent, i.e. fish sampled during 2013 and analyses finalised in 2014. Compared to the 2006 VKM report, the contaminants and nutrients in Atlantic salmon fillet have changed as described in Chapter 5, and summarised here;
 - In the 2006 VKM report nutrient data for farmed Atlantic salmon were; 8 µg vitamin D per 100 g, 30 µg selenium per 100 g, 6-34 µg iodine per 100 g, 520 mg n-6/100 g, 3200 mg n-3/100 g, and 2700 mg/100 g EPA+DPA+DHA.
 - In the current VKM report nutrient data for farmed Atlantic salmon were; 7.5 µg vitamin D per 100 g, 12 µg selenium per 100 g, 4 µg iodine per 100 g, 2296 mg n-6 per 100 g, 2303 mg n-3 per 100 g, and 1311 mg per 100 g EPA+DPA+DHA.
 - In the 2006 VKM report, contaminant data for farmed Atlantic salmon were; 0.030 mg/kg mercury, 1.7 ng dioxins and dl-PCBs TEQ/kg, 1.2 ng dl-PCBs TEQ/kg, and 0.5 ng dioxins TEQ/kg.
 - In the current VKM report, contaminant data for farmed Atlantic salmon were; 0.014 mg/kg mercury, 0.52 ng dioxins and dl-PCBs TEQ/kg, 0.28 ng dl-PCBs TEQ/kg, and 0.24 ng dioxins TEQ/kg.

For concentrations of nutrients and contaminants used in the intake and exposure assessment in Chapter 7, see Appendix VII.

7 Intake and exposure assessment

7.1 Current intake and exposure assessment from fish consumption

The assessments of intake of nutrients and exposure to contaminants in the Norwegian population from fish consumption have been performed on three different population groups: 2-year-olds, pregnant women and adults 18-70 years of age. The dietary surveys are conducted with different dietary assessment methods. The fish consumption data which is the basis for calculating nutrient intakes and contaminant exposures are described in Chapter 3. A short overview of consumption data is given in Table 7.1-1. For concentrations used in the calculations of nutrient intake and contaminant exposure, see Appendix VII. The basis for the occurrence data in Appendix VII is shown in Chapter 6.

As can be seen from table 7.1-1, the difference between median and mean total fish intake is much larger in adults (Norkost 3) than in both 2-year olds (Småbarnskost 2007) and pregnant women (MoBa). Likewise, the 95th percentile fish intake in adults is almost 4-fold higher than the mean, whereas the 95th percentile consumption in 2-years-olds and in pregnant women is 2.2-fold. Because of the method used in Norkost 3 (two 24-hour recalls), the 95th percentile represents participants reporting fish for dinner on both recall days. This represents an overestimation of the weekly fish consumption in high consumers, because having fish for dinner two recall days reported one month apart, does not imply that they consume fish for dinner all days of a week. Likewise, the median most likely underestimates the long term fish consumption, because it is influenced by those who did not have fish for dinner any of the recall days, but usually eat fish on a weekly basis. Because of the large number of participants mean consumption can be used for comparison between the dietary surveys. The interpretation of the 95th percentile intake estimates for nutrients and the 95th percentile exposure estimates for contaminants is affected by the above described overestimation, and illustrates major reasons why direct comparisons between high intakes and exposures between the surveys conducted with different methods should not be done.

The combined average fish consumption of both gender have been used for estimation of intake of nutrients and exposure to contaminants, although consumption differs by gender (i.e. men eat in general more than women). This leads to underestimation of nutrient contributed by fish in men, and to an overestimation in women. However, whereas intake of nutrients is given as amount per person, exposure to contaminants is assessed based on body weight in kilogram. Thus, the use of combined average fish consumption has minor implications for estimation of contaminant exposure.

Table 7.1-1 Fish consumption (g/day) in 2-year-olds (Småbarnskost 2007, n=1674), adults (Norkost 3, n=1787) and pregnant women (MoBa, n=86277)

Population groups	Fish, total			Lean fish, cod (≤5% fat)			Fatty fish (>5% fat)		
	Mean	Median	P95	Mean	Median	P95	Mean	Median	P95
2-year-olds	16	14	36	10	9	24	5	2	16
Adults^a	51	17	201	30	0 ^b	162	21	0 ^b	113
Pregnant women	31	27	68	18	16	41	11	7.3	36

^aMedians are considered an underestimate and 95th percentiles (P95) are considered an overestimate because of the dietary assessment method used.

^bMedian is zero because less than 50% of the participants were consumers.

7.1.1 Nutrient intake estimates from food consumption surveys

In the following, intake estimates have been done for the most important nutrients in fish; the n-3 LCPUFAs EPA, DPA and DHA, vitamin D, selenium and iodine. Intake estimates have also been included for the total sum n-3 in order to illustrate how much EPA, DPA and DHA constitute of sum n-3. Furthermore, even though fish is normally not an important source of n-6 PUFAs, the total sum of n-6 fatty acids has also been included since an increased use of vegetable oils in the feed for farmed fish has resulted in an increased concentration of n-6 PUFAs (Chapter 5).

7.1.1.1 Two-year-olds

In 2-year-olds, fish intake was assessed using a food frequency questionnaire; fish was consumed by nearly all (98%) (Chapter 3.2.1).

Polyunsaturated fatty acids (PUFAs); focus on eicosapentaenoic acid (EPA), docosahexaenoic acid (DPA) and docosapentaenoic acid (DHA)

The calculated intakes of fatty acids contributed by fish in 2-year-olds are presented in Table 7.1.1.1-1.

Table 7.1.1.1-1 Intake of fatty acids from fish in 2-year-olds (Småbarnskost 2007, n=1674), presented as contribution from total fish intake and the subgroups lean fish, fatty fish and fish roe and liver

Food item	Sum EPA+DPA+DHA mg/day			Sum n-3 mg/day			Sum n-6 mg/day		
	Mean	Median	P95	Mean	Median	P95	Mean	Median	P95
Fish, total, n=1674	204	89	696	300	125	1047	52	34	159
Lean fish (≤5% fat)^a	28	24	66	29	25	69	2.3	2.0	5.4
Cod, saithe	4.9	2.7	17	5.0	2.8	17	0.39	0.22	1.3
Fish balls, fish pudding	8.1	6.0	25	8.4	6.2	26	0.65	0.48	2.0
Fish au gratin	2.2	1.2	7.6	2.3	1.2	7.9	0.18	0.10	0.62
Fish burgers	7.8	5.4	23	8.1	5.6	24	0.63	0.44	1.8
Fish fingers	4.5	2.6	17	4.6	2.7	17	0.36	0.21	1.3
Jarred baby food w/fish	0.60	0 ^c	<0.01	0.62	0 ^c	<0.01	0.05	0 ^c	<0.01

Food item	Sum EPA+DPA+DHA mg/day			Sum n-3 mg/day			Sum n-6 mg/day		
	Mean	Median	P95	Mean	Median	P95	Mean	Median	P95
Fatty fish (>5% fat)	165	38	631	254	67	959	50	33	156
Salmon (farmed)	17	7.7	54	30	14	94	30	14	94
Mackerel in tomato sauce	148	0 ^c	615	224	0 ^c	930	20	0 ^c	84
Fish roe and liver	11	0 ^c	22	16	0 ^c	52	na	na	na
Cod roe and liver pâté	8.1	0 ^c	- ^b	9.7	0 ^c	- ^b	na	na	na
Roe (in caviar)	2.8	0 ^c	12	6.5	0 ^c	29	na	na	na

na: no data available for content of fatty acids, ^aOnly raw fish content from the different food products are included, mostly cod, ^bP95= 95th percentile; was not calculated due to less than 60 consumers, ^cMedian was zero because less than 50% of the participants had consumed the fish/fish product.

In 2-year-olds, total fish consumption contributed on average 204 mg EPA+DPA+DHA per day, the median was 89 mg and high consumption (95th percentile) was 696 mg/day. Lean fish contributed on average 14%, fatty fish contributed 81% and cod roe and liver contributed 5% to the total intake of EPA+DPA+DHA. Mackerel in tomato sauce was the major contributor to fatty fish. Fatty fish also contributed most to the intake of sum n-3 PUFA (85%) and sum n-6 PUFA (96%) in 2-year-olds from fish.

Vitamin D, iodine and selenium

The calculated intake of vitamin D, iodine and selenium from fish in 2-year-olds are presented in Table 7.1.1.1-2.

Table 7.1.1.1-2 Intake of vitamin D, iodine and selenium from fish in all 2-year-olds (Småbarnskost 2007, n=1674), presented as contribution from total fish intake and the subgroups lean fish, fatty fish and fish roe and liver

Food item	Vitamin D µg/day			Iodine µg/day			Selenium µg/day		
	Mean	Median	P95	Mean	Median	P95	Mean	Median	P95
Fish, total (n=1674)	0.51	0.36	1.3	35	31	82	4.5	3.5	12
Lean fish (≤5% fat)^a	0.14	0.13	0.34	33	29	79	2.5	2.2	5.8
Cod, saithe ^b	0.03	0.01	0.09	5.8	3.2	20	0.43	0.24	1.5
Fish balls, fish pudding ^b	0.04	0.03	0.13	9.6	7.1	30	0.71	0.53	2.2
Fish au gratin ^b	0.01	0.01	0.04	2.6	1.4	9.0	0.19	0.11	0.67
Fish burgers ^b	0.04	0.03	0.12	9.2	6.4	27	0.69	0.48	2.0
Fish fingers ^b	0.02	0.01	0.09	5.3	3.1	20	0.39	0.23	1.5
Jarred baby food w/fish ^b	<0.01	0 ^c	<0.01	0.71	0 ^c	<0.01	0.05	0 ^c	<0.01
Fatty fish (>5% fat)	0.19	0.14	0.65	0.62	0.12	2.4	1.9	0.34	7.3
Salmon (farmed)	0.10	0.04	0.31	0.05	0.02	0.16	0.16	0.07	0.49
Mackerel	0.09	0 ^c	0.39	0.57	0 ^c	2.3	1.7	0 ^c	7.2
Fish roe and liver	0.17	0 ^c	0.89	1.3	0 ^c	7.7	0.17	0 ^c	0.66
Cod roe and liver pâté	0.06	0 ^c	- ^b	0.35	0 ^c	- ^d	0.08	0 ^c	- ^d
Roe (in caviar)	0.11	0 ^c	0.50	0.97	0 ^c	4.3	0.08	0 ^c	0.37

^aAll lean fish is defined as cod,

^bOnly raw fish content from the different food products are included,

^cMedian was zero because less than 50% of the participants had consumed the fish/fish product,

^d95th percentile (P95) was not calculated due to less than 60 consumers.

In the **2-year-olds**, fish consumption contributed on average with 0.51 µg **vitamin D** per day, the median was 0.36 and high consumption (95th percentile) was 1.3 µg/day. Although fatty fish has higher concentration of vitamin D, vitamin D contributed by fish in this age group originated both from fatty fish (38%) and lean fish (28%), as well as from cod roe and liver (34%).

Fish consumption contributed on average with 35 µg **iodine** per day, the median was 31 µg and high consumption (95th percentile) contributed 82 µg/day. Nearly all (95%) iodine contributed by fish originated from lean fish.

Fish consumption contributed on average with 4.5 µg **selenium** per day, the median was 3.5 µg and high consumption (95th percentile) contributed 12 µg. Selenium contributed by fish consumption originated both from lean and fatty fish (56% and 42%, respectively).

Intake of nutrients from fish oil and cod liver oil in 2-year-olds

Fish oil and cod liver oil supplements were given to 41% of the 2-year-olds. Fish oil and cod liver oil supplements contribute substantially with fatty acids and vitamin D only among those who are consumers. For illustrating this, the contribution in consumers only (i.e. only among those reported consumption) has been calculated. The average contribution of EPA+DPA+DHA from supplements in all participating 2-year-olds was 454 mg/day (Table 7.1.1.1-3). Among users of fish oil and cod liver oil supplement, the supplements contributed on average with 1103 mg/day (Table 7.1.1.1-4). Vitamin D contributed by fish oil and cod liver oil was on average 3.2 µg/day in all participants and 7.8 µg in supplement users. Sum EPA, DPA and DHA amounted 83% of sum n-3 PUFA.

Table 7.1.1.1-3 Intake of fatty acids and vitamin D from fish oil and cod liver oil in 2-year-olds (Småbarnskost 2007, n=1674)

Supplement	Sum EPA, DPA and DHA mg/day		Sum n-3 mg/day		Vitamin D µg/day	
	Mean	P95	Mean	P95	Mean	P95
Fish oil and cod liver oil^a n=1674	454	1779	545	2136	3.2	13

P95 = 95th percentiles. ^aFor intake estimates of nutrients, data for fish oil and cod liver oil were combined, and a weighted mean was used.

Table 7.1.1.1-4 Intake of fatty acids and vitamin D from fish oil and cod liver oil in 2-year-olds (Småbarnskost 2007), for consumers only (n=689)

Supplement	Sum EPA+DPA+DHA mg/day			Sum n-3 mg/day			Vitamin D µg/day		
	Mean	Median	P95	Mean	Median	P95	Mean	Median	P95
Fish oil and cod liver oil^a, n=689	1103	1271	1805	1325	1526	2167	7.8	9.0	13

P95 = 95th percentiles. ^aFor intake estimates of nutrients, data for fish oil and cod liver oil were combined, and a weighted mean was used.

A daily intake of 5 ml fish oil and cod liver oil (manufacturer's recommendation) would contribute a mean intake of 1280 mg EPA+DPA+DHA and 10 µg vitamin D per day.

7.1.1.2 Adults

In adults, fish intake was assessed using two 24-hour recalls by telephone at least one month apart (Chapter 3, Table 3.2.2-2). Fish was consumed by 61% of all participants. The intake of nutrients contributed by fish was presented as combined mean of both sexes. Furthermore, the percentage of consumers for each fish or fish product was below 50% and thus the median was not presented in the following tables, but the medians for total fish intakes are presented in the text (see the introduction of this chapter).

Polyunsaturated fatty acids (PUFAs); focus on eicosapentaenoic acid (EPA), docosahexaenoic acid (DPA) and docosapentaenoic acid (DHA)

The calculated intakes of fatty acids from fish in adults are presented in Table 7.1.1.2-1.

Table 7.1.1.2-1 Intake of fatty acids from fish in adults (Norkost 3, n=1787), presented as contribution from total fish intake and the subgroups lean fish, fatty fish and cod roe and liver. Mean is the mean of two 24-hour recalls

Food item	Sum EPA+DPA+DHA mg/day		Sum n-3 mg/day		Sum n-6 mg/day	
	Mean	P95	Mean	P95	Mean	P95
Fish, total, n=1787	475	2132	713	3248	339	2066
Lean fish (≤ 5% fat)	82	452	86	474	6.7	36
Saithe	14	- ^c	15	- ^c	0.9	- ^c
Cod	65	384	67	396	5.2	31
Haddock	na	na	na	na	na	na
Plaice	2.9	- ^a	3.3	- ^a	0.3	- ^a
Redfish	na	na	na	na	na	na
Wolffish	0.5	- ^a	0.5	- ^a	0.3	- ^a
Tuna	na	na	na	na	na	na
Fatty fish (> 5% fat)	375	1904	603	3052	332	2043
Herring (Norwegian spring spawning)	23	149	30	199	2.3	15
Halibut	4.8	- ^a	5.5	- ^a	0.6	- ^a
Mackerel	167	1353	252	2046	23	184
Salmon (wild)	6.3	- ^a	7.6	- ^a	0.7	- ^a
Trout (freshwater)	na	na	na	na	na	na
Salmon (farmed) ^b	175	1142	307	2005	306	1999
Fish roe and liver	17	20	25	47	0.4	-^a
Cod roe	3.8	16	8.8	38	na	na
Cod roe and liver paté	10	- ^a	13	- ^a	na	na
Cod liver	3.1	- ^a	3.7	- ^a	0.4	- ^a

na: no data available for fatty acid content in the food item.

^a95th percentiles (P95) are considered an overestimate because of the dietary survey method used.

^bFarmed salmon includes farmed trout both with respect to consumption and level of fatty acids.

^c95th percentile (P95) are zero, due to less than 5% consumers.

In adults, total fish consumption contributed on average with 475 mg EPA+DPA+DHA per day, the median was 101 mg and high consumption (95th percentile) was 2.1 g/day. Lean fish contributed on

average with 17%, fatty fish with 79% and cod roe and liver with 4% of EPA+DPA+DHA from fish. Of the fatty fish species, farmed salmon and mackerel were the major sources. Fatty fish (salmon and mackerel) was the main contributor to sum n-3 PUFA (84%), and salmon was the main contributor to sum n-6 (98%). Median intakes of sum n-3 PUFA and sum n-6 PUFA from total fish consumption in adults were 119.3 mg/day and 7.96 mg/day, respectively.

Vitamin D, iodine and selenium

The calculated intakes of vitamin D, iodine and selenium in adults are presented in Table 7.1.1.2-2.

Table 7.1.1.2-2 Intake of vitamin D, iodine and selenium from fish in adults (Norkost 3, n=1787), presented as contribution from total fish intake and the subgroups lean fish, fatty fish and cod roe and liver. Mean is the mean of two 24-hour recalls.

Food item	Vitamin D µg/day		Iodine µg/day		Selenium µg/day	
	Mean	P95	Mean	P95	Mean	P95
Fish, total, n=1787	2.1	10	86	475	15	59
Lean fish (≤5% fat)	0.44	2.3	82	466	10	48
Saithe	0.05	- ^c	5.1	- ^c	1.0	- ^c
Cod	0.33	2.0	77	454	5.7	34
Haddock	<0.01	- ^a	na	na	0.13	- ^a
Plaice	0.03	- ^a	0.07	- ^a	0.16	- ^a
Redfish	na	na	na	na	0.28	- ^a
Wolffish	<0.01	- ^a	0.27	- ^a	0.06	- ^a
Tuna	0.02	- ^a	0.12	- ^a	3.1	- ^a
Fatty fish (>5% fat)	1.4	8.7	1.4	6.8	4.5	22
Herring (Norwegian spring spawning)	0.20	1.3	0.03	0.18	0.80	5.2
Halibut	0.09	- ^a	0.14	- ^a	na	na
Mackerel	0.10	0.85	0.64	5.2	1.9	16
Salmon (wild)	0.04	- ^a	0.05	- ^a	0.16	- ^a
Trout (freshwater)	na	na	na	na	na	na
Salmon (farmed) ^b	1.0	6.5	0.53	3.5	1.6	10
Fish roe and liver	0.25	0.82	1.9	7.0	0.25	0.61
Cod roe	0.15	0.65	1.3	5.6	0.11	0.49
Cod roe and liver paté	0.07	- ^a	0.45	- ^a	0.11	- ^a
Cod liver	0.02	- ^a	0.10	- ^a	0.02	- ^a

na: no data available for mineral content in the food item.

95th percentiles (P95) are considered an overestimate because of the dietary survey method used.

^a95th percentile (P95) was not calculated due to less than 60 consumers.

^bFarmed salmon includes farmed trout both with respect to consumption and level of fatty acids.

In adults, fish consumption contributed on average with 2.1 µg vitamin D per day, the median was 0.56 µg/day, and for high consumption (95th percentile) the contribution was 10 µg/day. The fish items contributing most to vitamin D were farmed salmon (47%), cod (15%) and herring (9%).

Fish consumption contributed on average with 86 µg iodine per day, median was 2.3 µg and high consumption (95th percentile) contributed 475 µg/day in adults. Lean fish was the

source of nearly all iodine contributed by fish. The large difference between mean (86 µg) and median (2.3 µg) is due to one participant with exceptionally high consumption of lean fish in the 24-h recalls.

Fish consumption contributed on average with 15 µg selenium per day the median was 4.2 µg and high consumption (95th percentile) contributed 59 µg/day in adults. In adults, the lean species contributed a larger proportion of selenium than fatty fish (67% and 30%, respectively).

Intake of nutrients from fish oil and cod liver oil in adults

Fish oil and cod liver oil supplements were used by 37% of the adults during the two 24-hour recalls, and the average contribution of EPA+DPA+DHA from supplements in all participants was 735 mg/day (Table 7.1.1.2-3). Sum EPA, DPA and DHA amounted 83-84% of sum n-3 PUFA. For fish oil and cod liver oil supplement users only, the supplements contributed on average with 1982 mg/day and high intake (95th percentile) was 3000 mg/day (Table 7.1.1.2-4). A daily intake of 5 ml fish oil and cod liver oil (manufacturer's recommendation) would contribute a mean intake of 1280 mg EPA + DPA + DHA per day.

Vitamin D contributed by fish oil and cod liver oil was on average 3.5 µg/day in all participants (Table 7.1.1.2-3) and 9.4 µg/day in supplement users (Table 7.1.1.2-4). A daily intake of 5 ml fish oil and cod liver oil (manufacturer's recommendation) would contribute a mean intake of Vitamin D of 10 µg/day.

Table 7.1.1.2-3 Intake of fatty acids from fish oil and cod liver oil in adults, all participants (Norkost 3, n=1787)

Supplement	Sum EPA+DPA+DHA mg/day		Sum n-3 mg/day		Vitamin D µg/day	
	Mean	P95	Mean	P95	Mean	P95
Fish oil and cod liver oil^a, n=1787	735	2796	880	3346	3.5	13

P95: 95th percentiles. ^aFor intake estimates of nutrients, data for fish oil and cod liver oil were combined, and a weighted mean was used.

Table 7.1.1.2-4 Intake of fatty acids from fish oil and cod liver oil in adults, consumers only (Norkost 3, n=663)

Supplement	Sum EPA+DPA+DHA mg/day		Sum n-3 mg/day		Vitamin D µg/day	
	Mean	P95	Mean	P95	Mean	P95
Fish oil/cod liver oil^a, n=663	1982	2999	2372	3589	9.4	14

P95: 95th percentiles. ^aFor intake estimates of nutrients, data for fish oil and cod liver oil were combined, and a weighted mean was used.

7.1.1.3 Pregnant women

As described in Chapter 3.2.3, data for pregnant women are derived from studies within the national Mother and Child Cohort Study (MoBa). Fish was consumed by nearly all participants (97%).

Polyunsaturated fatty acids (PUFAs); focus on eicosapentaenoic acid (EPA), docosahexaenoic acid (DPA) and docosapentaenoic acid (DHA)

The calculated intakes of fatty acids from fish in pregnant women are presented in Table 7.1.1.3-1.

Table 7.1.1.3-1 Intake of fatty acids from fish in pregnant women (MoBa, n=86277)

Food item	Sum EPA+DPA+DHA mg/day			Sum n-3 mg/day			Sum n-6 mg/day		
	Mean	Median	P95	Mean	Median	P95	Mean	Median	P95
Fish, total	312	200	992	464	293	1497	143	114	392
Lean fish (≤5% fat)	48	43	114	50	44	119	4.1	3.5	9.8
Cod, saithe, haddock	40	35	97	42	36	100	3.2	2.8	7.8
Redfish, catfish	3.5	0 ^a	19	3.7	0 ^a	20	0.28	0 ^a	1.5
Pike, perch	<0.01	0 ^a	0	<0.01	0 ^a	0	<0.01	0 ^a	0
Tuna	na	na	na	na	na	na	na	na	na
Halibut, flatfish	4.4	0 ^a	27	5.0	0 ^a	31	0.53	0 ^a	3.2
Fatty fish (>5% fat)	251	140	901	395	229	1387	139	110	386
Mackerel, herring	186	73	828	281	110	1252	25	9.9	112
Salmon, trout ^b	65	50	191	114	87	336	114	87	335
Fish roe and liver	13	0^a	37	19	0^a	65	0.08	0^a	0
Cod roe	2.8	0 ^a	15	6.6	0 ^a	36	<0.01	0 ^a	0
Cod roe and liver pate	9.2	0 ^a	0	11	0 ^a	0	<0.01	0 ^a	0
Cod liver	0.7	0 ^a	0	0.85	0 ^a	0	0.08	0 ^a	0

na: No data available for fatty acids in the food item.

^aMedian was zero because less than 50% of the participants had consumed the fish/fish product.

^bFarmed salmon represent salmon and trout with respect to consumption and content of fatty acids.

In pregnant women, mean total fish consumption contributed with 312 mg EPA+DPA+DHA per day, median was 200 and high consumption (95th percentile) 990 mg/day. Fatty fish contributed 80% of EPA+DPA+DHA, and of the fatty fish species, mackerel and herring contributed substantially more EPA+DPA+DHA and sum n-3 PUFA than salmon and trout. Sum EPA+DPA+DHA amounted about 66-68% of sum n-3 PUFA. Fatty fish was also the main contributor to sum n-6 from fish (97%) and salmon and trout contributed most (80%).

Vitamin D, iodine and selenium

The calculated intakes of vitamin D, selenium and iodine from fish in pregnant women are presented in Table 7.1.1.3-2.

Table 7.1.1.3-2 Intake of vitamin D, selenium and iodine from fish in pregnant women (MoBa, n=86277)

Food tem	Vitamin D µg/day			Iodine µg/day			Selenium µg/day		
	Mean	Median	P95	Mean	Median	P95	Mean	Median	P95
Fish, total, n=86277	0.96	0.79	2.3	54	48	127	9.0	7.0	23
Lean fish (≤5% fat)	0.29	0.24	0.69	52	46	123	6.1	4.6	16
Cod, saithe, haddock	0.21	0.18	0.50	48	42	114	3.5	3.1	8.5
Redfish, catfish	0.02	0 ^a	0.10	4.2	0 ^a	23	0.31	0 ^a	1.7
Pike, perch	<0.01	0 ^a	0	<0.01	0 ^a	0	0.01	0 ^a	0
Tuna	0.02	0 ^a	0.08	0.08	0 ^a	0.42	2.0	0 ^a	10
Halibut, flatfish	0.05	0 ^a	0.28	0.10	0 ^a	0.61	0.24	0 ^a	1.5
Fatty fish (>5% fat)	0.49	0.39	1.4	0.91	0.48	3.4	2.8	1.4	10
Mackerel, herring	0.12	0.05	0.53	0.71	0.28	3.2	2.2	0.85	9.7
Salmon, trout	0.37	0.28	1.1	0.20	0.15	0.58	0.59	0.45	1.8
Fish roe and liver	0.18	0 ^a	0.79	1.4	0 ^a	6.2	0.09	0 ^a	0.50
Cod roe	0.11	0 ^a	0.62	0.98	0 ^a	5.3	0.09	0 ^a	0.46
Cod roe and liver pate	0.12	0 ^a	0.66	0.39	0 ^a	0	0.19	0 ^a	0.68
Cod liver	0.01	0 ^a	0	0.02	0 ^a	0	0.01	0 ^a	0

P95: 95th percentiles. ^aMedian was zero because less than 50% of the participants had consumed the fish or fish product

In pregnant women, fish contributed on average 0.96 µg **vitamin D**, the median was 0.79 µg and high consumption was 2.3 µg/day. Fatty fish contributed 51% of vitamin D from fish, with salmon being the most influential contributor. Lean fish and cod roe also contributed to vitamin D from fish in pregnant women (30% and 19%, respectively).

Fish contributed on average 54 µg **iodine** per day, the median was 48 µg and high consumption (95th percentile) was 127 µg/day in pregnant women. Iodine contributed by fish originated almost completely from lean fish species (96%).

Fish contributed on average 9 µg **selenium** per day, the median was 7 µg and high consumption (95th percentile) was 23 µg/day in pregnant women. Selenium contributed by fish originated mostly from lean fish (68%).

Intake of nutrients from fish oil and cod liver oil in pregnant women

Nutrients contributed by fish oil and cod liver oil have not been estimated for the current update. However, a sub-study in nulliparous women enrolled in MoBa during the years 2002 to 2005 estimated that the median amount of EPA+DHA contributed by fish oil and cod liver oil supplements was 190 mg/day (Haugen et al., 2009).

A daily intake of 5 ml cod liver oil (manufacturer's recommendation) would contribute with a mean intake of 1280 mg EPA+DPA+DHA per day. Furthermore, this would also contribute with a mean intake of vitamin D of 10 µg/day.

7.1.2 Summary of current nutrient intake from food consumption surveys

Polyunsaturated fatty acids (PUFAs); focus eicosapentaenoic acid (EPA), docosahexaenoic acid (DPA) and docosapentaenoic acid (DHA)

In **2-year-olds**, the mean intake of EPA+DHA+DPA contributed by fish is 204 mg EPA+DPA+DHA per day and the 95th percentile 696 mg/day. **In adults**, the amount of EPA+DPA+DHA from mean total fish intake is approximately 475 mg/day, and the 95th percentile is 2132 mg/day. **In pregnant** women the mean estimated intake of EPA+DHA+DPA is 312 mg per day, and the 95th percentile is 992 mg/day. The major contributors to EPA+DHA+DPA from fatty fish were mackerel in tomato sauce, mackerel (1/2) and farmed salmon (1/2), and mackerel (2/3) and farmed salmon (1/3), in 2-year-olds, adults and pregnant women, respectively.

EPA+DHA+DPA from fish constituted between 70-80% of sum n-3 PUFAs for all age groups, and above 80% for fish and cod liver oils. The main contributor of sum n-6 PUFAs was fatty fish for all age groups; farmed salmon in adult and pregnant women, and farmed salmon and mackerel for the 2-year olds.

The main source of EPA+DHA+DPA is fatty fish, besides fish oil and cod liver oil which is consumed by a relative large part of two of the populations (41% of the 2-year-olds and 37% of the adults, Figure 7.1.2-1).

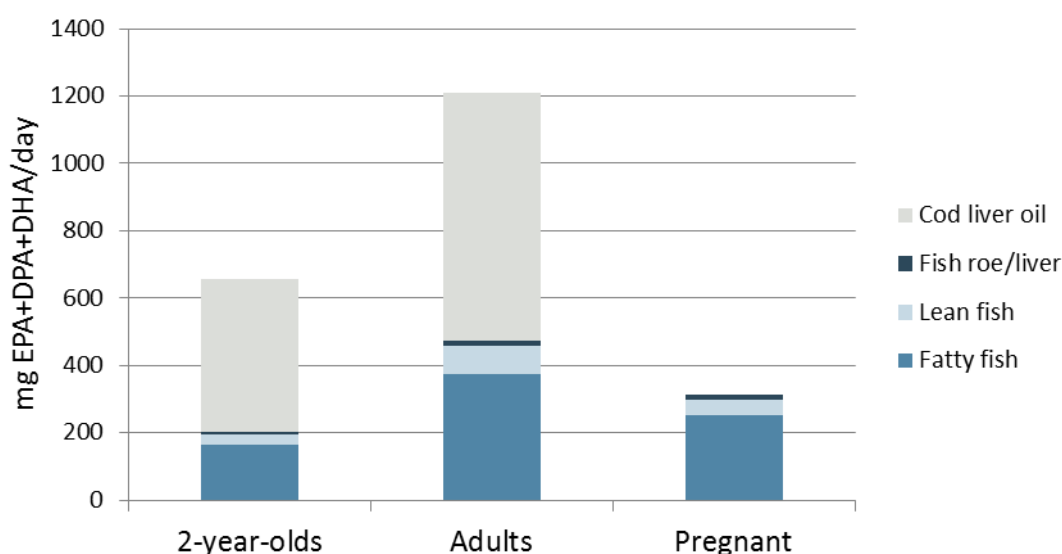


Figure 7.1.2-1 Mean intake of EPA+DPA+DHA from fish, and cod liver oil (including fish oil) in Norwegian 2-year-olds (Småbarnskost, 2007), adults (Norkost 3) and in pregnant women (MoBa, not including cod liver oil). Fish is grouped into fatty fish, lean fish, and fish roe and liver

Vitamin D

Vitamin D contributed by fish in **2-year-olds** and **adults** are on average 0.51 and 2.1 µg/day, respectively. In **pregnant women**, the mean vitamin D intake is 0.96 µg/day. The main source for vitamin D is fatty fish, besides fish oil and cod liver oil which is consumed by a relatively large part of two of the populations (41% of the 2-year-olds and 37% of the adults Figure 7.1.2-2).

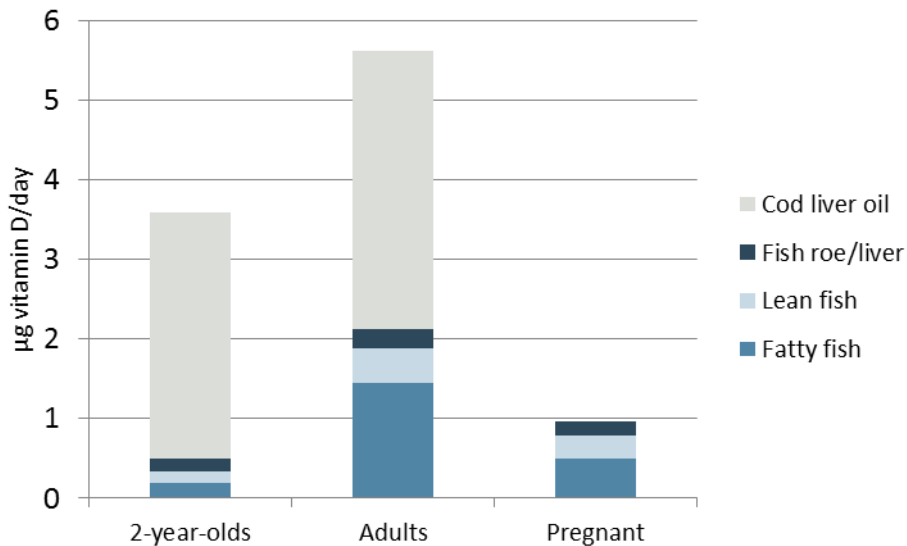


Figure 7.1.2-2 Mean intake of vitamin D from fish, and cod liver oil (including fish oil) in 2-year-olds (Småbarnskost 2007), adults (Norkost 3) and in pregnant women (MoBa, not including cod liver oil). Fish is grouped into fatty fish, lean fish, fish roe and liver, and cod liver oil.

Iodine, selenium

In 2-year-olds average fish consumption contributes with 35 µg iodine per day. In adults the mean intake is 86 µg iodine per day from fish and in pregnant women 54 µg/day. Lean fish is the main source for iodine (Figure 7.1.2-3).

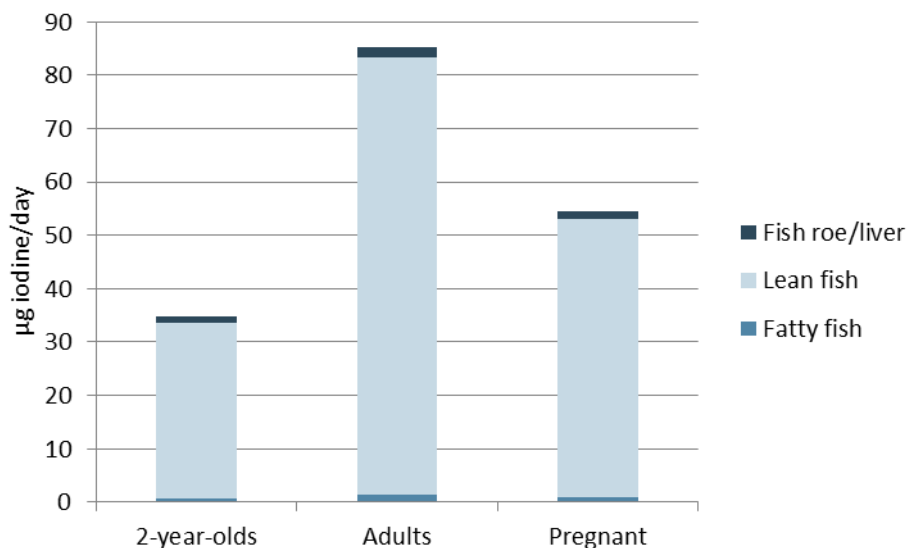


Figure 7.1.2-3 Mean intake of iodine from fish in 2-year-olds (Småbarnskost 2007, adults (Norkost 3) and in pregnant women (MoBa). Fish is grouped into fatty fish, lean fish, fish roe and liver.

In **2-year-olds** the contribution of selenium from average fish consumption is 4.5 µg/day. In **adults** the mean selenium intake from fish is 15 µg per day and in **pregnant women** 9 µg/day. The selenium concentration is about the same in lean and fatty fish (Figure 7.1.2-4).

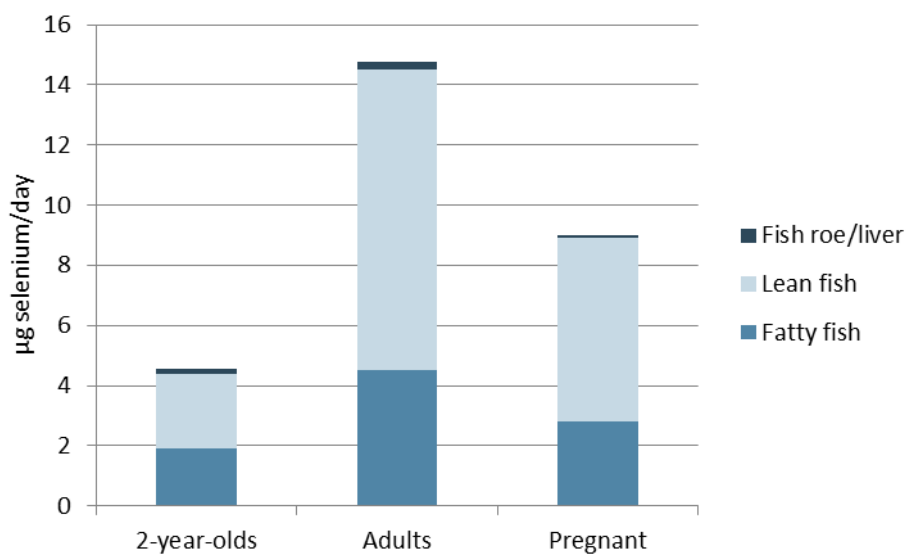


Figure 7.1.2-4 Mean intake of selenium from fish in Norwegian 2-year-olds (Småbarnskost 2007), adults (Norkost 3) and in pregnant women (MoBa). Fish is grouped into fatty fish, lean fish, fish roe and liver.

7.1.3 Contaminant exposure estimates from food consumption surveys

In the present chapter, the exposure assessments of mercury and dioxins through fish consumption have been presented in tables as mean and 95th percentile of both upper and lower bound for the three different population groups (2-year-olds, adults, and pregnant women), and median exposure have been given for 2-year-olds and pregnant women. Upper bound (UB) is when the concentrations lower than the limit of quantification (LOQ) or limit of detection (LOD) is substituted with the LOQ or LOD. This most likely represents an overestimate of the exposure. For lower bound (LB), concentrations lower than the LOQ or LOD is substituted with 0. This most likely represents an underestimate of the exposure.

For mercury there are small differences between lower bound and upper bound estimates because concentration in most samples has been quantified. Therefore, the description on mercury exposure in the text is based on upper bound estimates. For dioxins and dl-PCBs the uncertainty in concentrations in fish is higher and in order to reflect this, both upper- and lower bound results are described also in the text.

Total mercury analysed in fish is regarded as methylmercury. This is a conservative estimate since reports indicate that methylmercury generally constitutes 80-100% of total mercury in fish (EFSA, 2012a).

For the concentrations used in the calculations of contaminant exposure, the reader is advised to Appendix VII "Concentrations of nutrients and contaminants used in the exposure estimates".

7.1.3.1 Body weights used in contaminant exposure calculations

Exposure to contaminants is calculated per kilo body weight (in contrast to intake of nutrients). In this chapter, the individual body weights reported in the different dietary surveys (Chapter 3) have been used. In individuals who have not reported their body weight, exposure calculations have been based on mean body weight in the group. Among the 2-year-olds, 37% (n=620) were given the group mean body weight of 12.8 kg. In Norkost 3, only 1.7% (n=20) of the adults did not report their body weight, and were given the group mean body weight of 77.5 kg. In the MoBa study the group, individual pre-pregnancy body weight was used. Of the 86277 MoBa participants body weights were not reported for 2494, thus exposure to contaminants has been based on 83782 participants.

7.1.3.2 Two-year-olds

Mercury

Calculated mercury exposure from fish in 2-year-olds is shown in Table 7.1.3.2-1. Mean mercury UB exposure from fish was 0.51 µg/kg bw/week and high UB (95th percentile) exposure was 1.2 µg/kg bw/week. Lean fish contributed with 84% to the mean exposure.

The lean fish was mainly consumed in the form of fish balls/pudding, fish burger and fish fingers.

Table 7.1.3.2-1 Exposure to mercury from fish in 2-year-olds (Småbarnskost 2007, n=1674)

Food item	Lower bound µg Hg/kg bw/week			Upper bound µg Hg/kg bw/week		
	Mean	Median	P95	Mean	Median	P95
Fish, total (n=1674)	0.50	0.44	1.1	0.51	0.45	1.2
Lean fish (cod) (≤5% fat)	0.42	0.37	1.0	0.42	0.37	1.0
Cod, saithe	0.07	0.04	0.25	0.07	0.04	0.25
Fish balls, fish pudding	0.12	0.09	0.38	0.12	0.09	0.38
Fish au gratin	0.03	0.02	0.11	0.03	0.02	0.11
Fish burgers	0.12	0.08	0.35	0.12	0.08	0.35
Fish fingers	0.07	0.04	0.25	0.07	0.04	0.25
Jarred baby food w/fish	<0.01	0 ^b	<0.01	0.01	0 ^b	<0.01
Fatty fish (> 5% fat)	0.08	0.02	0.31	0.08	0.02	0.31
Salmon, farmed	0.01	<0.01	0.04	0.01	<0.01	0.04
Mackerel	0.07	0 ^b	0.29	0.07	0 ^b	0.29
Fish roe and liver	0	0 ^b	<0.01	<0.01	0 ^b	0.03
Cod roe and liver pâte	0	0 ^b	- ^a	<0.01	0 ^b	- ^a
Roe (in caviar)	0	0 ^b	<0.01	<0.01	0 ^b	0.02

^a95th percentile (P95) was not calculated due to less than 60 consumers.

^bMedian was zero because less than 50% of the participants had consumed the fish or fish product.

Dioxins and dl-PCBs

Calculated exposure to dioxins and dl-PCBs in 2-year-olds is shown in Table 7.1.3.2-2. Total exposure to dioxins and dl-PCBs from fish was at mean lower bound (LB) 2.0 pg TEQ/kg bw/week and at mean upper bound (UB) 2.6 pg TEQ/kg bw/week. High exposure from fish (95th percentile) was at LB 7.3 pg TEQ/kg bw/week and at UB 9.4 pg TEQ/kg bw/week. Fatty fish was the major contributor (72%). Among fatty fish species, mackerel was the major contributor, reflecting a high mean consumption of mackerel in tomato sauce in this age group (mackerel 3 g/day versus farmed salmon 1 g/day, Table 3.2.1-1). Of note, cod roe and liver pate contributed with 17% of the total mean LB exposure, although the mean consumption was less than 1 g/day (Table 3.2.1-1). Exposure from other food than fish comes in addition.

Table 7.1.3.2-2 Exposure to dioxins and dl-PCBs from fish in 2-year-olds (Småbarnskost 2007, n=1674)

Food item	Lower bound Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week			Upper bound Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week		
	Mean	Median	P95	Mean	Median	P95
Fish, total, n=1674	2.0	0.93	7.3	2.6	1.3	9.4
Lean fish (cod) (≤5% fat)	0.20	0.17	0.47	0.32	0.27	0.75
Cod, saithe	0.03	0.02	0.12	0.05	0.03	0.19
Fish balls, fish pudding	0.06	0.04	0.18	0.09	0.06	0.28
Fish au gratin	0.02	0.01	0.05	0.02	0.01	0.09

Food item	Lower bound			Upper bound		
	Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week			Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week		
	Mean	Median	P95	Mean	Median	P95
Fish burgers	0.05	0.04	0.16	0.09	0.06	0.26
Fish fingers	0.03	0.02	0.12	0.05	0.03	0.19
Jarred baby food w/fish	<0.01	0 ^b	<0.01	<0.01	0 ^b	<0.01
Fatty fish (> 5% fat)	1.4	0.64	5.2	1.9	0.80	7.1
Salmon (farmed)	0.29	0.13	1.0	0.36	0.16	1.3
Mackerel	1.1	0 ^b	4.8	1.6	0 ^b	6.6
Fish roe and liver	0.36	0 ^b	0.13	0.36	0 ^b	0.13
Cod roe and liver pate	0.34	0 ^b	- ^c	0.34	0 ^b	- ^c
Roe (in caviar)	0.02	0 ^b	0.07	0.02	0 ^b	0.07

^aDioxins = polychlorinated dibenzo-para-dioxins (PCDD) and polychlorinated dibenzo furans (PCDF), dioxin-like (dl) PCBs (non-ortho and mono-ortho substituted PCBs).

^bMedian was zero because less than 50% of the participants had consumed the fish or fish product.

^c95th percentile (P95) was not calculated due to less than 60 consumers.

Exposure to contaminants from fish oils and cod liver oil in 2-year-olds

Since mercury is not associated with lipids, intake of mercury from fish oil and cod liver oil is very low and not of relevance.

Mean LB intake of dioxins and dl-PCBs from fish oil and cod liver oil among 2-year-olds was 0.24 pg TEQ/kg bw/week in all participants and 0.58 pg TEQ/kg bw/week in consumers only (Tables 7.1.3.2-3 and 7.1.3.2-4). For consumers only (41% of the participants), this constitutes 35% of the mean total exposure, and comes in addition to the exposure from fish and other food. As explained in Chapter 3, those who eat fish are more often consumers of fish oils or cod liver oil as supplement than those who do not eat fish regularly. The relatively high contribution from fish oil and cod liver oil in 2-year-olds compared to adults can be explained by the low body weight in children, and that the recommended daily volume of cod liver oil is similar for children and adults. Daily consumption of 5 ml fish oil or cod liver oil with a mean LB (UB) concentration of 0.27 (0.95) pg TEQ/g, corresponds to an exposure to dioxins and dl-PCBs of 0.66 (LB) to 2.34 (UB) pg TEQ/kg bw/week in 2-year-olds with mean body weight of 12.8 kg.

Table 7.1.3.2-3 Exposure of dioxins and dl-PCBs from fish oil and cod liver oil in 2-year-olds (Småbarnskost 2007, n=1674)

Supplement	Lower bound		Upper bound	
	Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week		Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week	
	Mean	P95	Mean	P95
Fish oil and cod liver oil^b, n=1674	0.24	0.93	0.84	3.3

P95: 95th percentiles.

^aDioxins = polychlorinated dibenzo-para-dioxins (PCDD) and polychlorinated dibenzo furans (PCDF). dl-PCBs - dioxin-like PCB (non-ortho and mono-ortho substituted PCBs).

^bFor exposure calculations data for fish oil and cod liver oil were combined and a weighed mean was used.

Table 7.1.3.2-4 Exposure to dioxins and dl-PCBs from fish oil and cod liver oil in 2-year-olds (Småbarnskost 2007), consumers only for fish oil and cod liver oil

Supplement	Lower bound			Upper bound		
	Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week			Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week		
	Mean	Median	P95	Mean	Median	P95
Fish oil and cod liver oil^b, n=689	0.58	0.59	1.0	2.0	2.1	3.7

P95: 95th percentiles.

^aDioxins = polychlorinated dibenzo-para-dioxins (PCDD) and polychlorinated dibenzo furans (PCDF). dl-PCBs - dioxin-like PCB (non-ortho and mono-ortho substituted PCBs).

^bFor exposure calculations data for fish oil and cod liver oil were combined and a weighed mean was used.

7.1.3.3 Adults

Mercury

Exposure to mercury from fish in adults (Norkost 3) is shown in Table 7.1.3.3-1. Mean exposure was 0.30 µg/kg bw/week. Lean fish contributed with 79% of the exposure, and cod was the main source among the lean fish species (Figure 7.1.3.3-1). This reflects merely the high consumption of cod, since the concentration of mercury in cod is not particularly high compared to less consumed species (Table 6.2-1). The median exposure from total fish was 0.036 (LB) and 0.041 (UB) µg/kg bw/week. The medians for individual fish species were zero because less than 50% were consumers.

7.1.3.3-1 Exposure to mercury (Hg) from fish in adults (Norkost 3, n=1787).

Food item	Lower bound		Upper bound	
	Mean	P95 ^a	Mean	P95 ^a
Fish, total	0.29	1.2	0.30	1.2
Lean fish (≤5% fat)	0.23	1.2	0.23	1.2
Saithe	0.02	0	0.02	0
Cod	0.16	0.95	0.16	0.95
Haddock	<0.01	- ^c	<0.01	- ^c
Plaice	0.03	- ^c	0.03	- ^c
Redfish	<0.01	- ^c	<0.01	- ^c
Wolffish	0	- ^c	<0.01	- ^c
Tuna	0.01	- ^c	0.01	- ^c
Fatty fish (>5% fat)	0.06	0.21	0.06	0.21
Herring (Norwegian spring spawning)	0.01	0.03	0.01	0.03
Halibut	0.019	- ^c	0.02	- ^c
Mackerel	0.013	0.10	0.01	0.10
Salmon (wild)	0.001	- ^c	<0.01	- ^c
Trout (freshwater)	0.005	- ^c	0.01	- ^c

Food item	Lower bound		Upper bound	
	Mean	P95 ^a	Mean	P95 ^a
Salmon (farmed) ^b	0.018	0.12	0.02	0.12
Fish roe and liver	<0.01	-. ^{cd}	<0.01	0.01
Cod roe	0 ^d	0 ^d	<0.01	0.01
Cod roe and liver paté	0 ^d	-. ^c	0	-. ^c
Cod liver	<0.01	-. ^c	<0.01	-. ^c

^a95th percentiles (P95) are considered an overestimate because of the dietary method used.

^bFarmed salmon includes exposure from farmed trout.

^c95th percentile (P95) was not calculated due to less than 60 consumers.

^dZero is used due to concentration values under limit of quantification.

Dioxins and dl-PCBs

Calculated exposure to dioxins and dl-PCBs in adults in Norkost 3 is shown in Table 7.1.3.3-2. Dioxins and dl-PCBs were found above the LOQ in most of the fatty fish samples, but not in all lean fish samples. Thus, the lower bound (LB) and upper bound (UB) intakes may differ for the lean fish species in particular. The mean LB exposure from all fish species was 1.4 pg TEQ/kg bw/week, whereas the mean UB exposure was 1.7 pg TEQ/kg bw/week. The median exposure from total fish was 0.18 (LB) and 0.26 (UB) pg TEQ/kg bw/week. The medians for individual fish species were zero because less than 50% were consumers. The 95th percentile exposure was at LB 5.6 pg TEQ/kg bw/week and at UB 6.8 pg TEQ/kg bw/week. As expected for lipid soluble contaminants as dioxins and dl-PCBs, fatty fish was the main source, contributing 76% of the exposure from fish. Farmed salmon contributed 36% of the mean exposure from fish. Exposure from other food than fish comes in addition.

7.1.3.3-2 Exposure to sum dioxins and dl-PCBs from fish in adults (Norkost 3, n=1787). Mean is the mean of two 24-hour recalls.

Food item	Lower bound		Upper bound	
	Mean	P95 ^b	Mean	P95 ^b
Fish, total (n=1787)	1.4	5.6	1.7	6.8
Lean fish (≤ 5% fat)	0.16	0.62	0.21	0.93
Saithe	0.02	<0.01	0.03	<0.01
Cod	0.08	0.45	0.12	0.71
Haddock	<0.01	-. ^c	<0.01	-. ^c
Plaice	0.01	-. ^c	0.01	-. ^c
Redfish	0.03	-. ^c	0.03	-. ^c
Wolffish	0.01	-. ^c	0.01	-. ^c
Tuna	No data	No data	No data	No data
Fatty fish (> 5% fat)	1.1	4.6	1.3	5.9
Herring (Norwegian spring spawning)	0.07	0.37	0.08	0.42
Halibut	0.31	-. ^c	0.32	-. ^c
Mackerel	0.22	1.7	0.30	2.3
Salmon (wild)	0.03	-. ^c	0.03	-. ^c
Trout (freshwater)	No data	No data	No data	No data
Salmon (farmed) ^d	0.50	3.4	0.63	4.2
Fish roe and liver	0.16	0.18	0.16	0.18

Food item	Lower bound Sum dioxins and dl-PCBs ^a pg TEQ/kg bw week		Upper bound Sum dioxins and dl-PCBs ^a pg TEQ/kg bw week	
	Mean	P95 ^b	Mean	P95 ^b
Cod roe	0.03	0.15	0.03	0.15
Cod roe and liver pate	0.08	- ^c	0.08	- ^c
Cod liver	0.05	- ^c	0.05	- ^c

^aDioxins = polychlorinated dibenzo-para-dioxins (PCDD) and polychlorinated dibenzo furans (PCDF), dioxin-like (dl) PCBs (non-ortho and mono-ortho substituted PCBs).

^b95th percentiles (P95) are considered an overestimate because of the dietary method used.

^c95th percentile (P95) was not calculated due to less than 60 consumers.

^dFarmed salmon includes exposure from farmed trout.

Exposure from fish oil and cod liver oil in adults

Since mercury is not associated with lipids, intake of mercury from fish oil and cod liver oil is very low and not of relevance.

Estimated intake of dioxins and dl-PCBs from fish oil in adults in Norkost 3 was low, as shown in Table 7.1.3.3-3, and the contribution to exposure compared with fish was low. This was also the case when mean intake was estimated among consumers only (Table 7.1.3.3-4). Daily consumption of 5 ml cod liver oil with a mean LB (UB) concentration of 0.27 (0.95) pg TEQ/g, would correspond to an exposure to dioxins and dl-PCBs of 0.11 (LB) to 0.39 (UB) pg TEQ/kg bw/week in adults with mean body weight of 77.5 kg.

Table 7.1.3.3-3 Exposure to dioxins and dioxin-like PCBs from fish oil and cod liver oil in adults (Norkost 3, n=1787)

Food item	Lower bound Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week		Upper bound Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week	
	Mean	P95	Mean	P95
Fish oil and cod liver oil^b, n=1787	0.1	0.3	0.3	0.9

P95: 95th percentiles.

^aDioxins = polychlorinated dibenzo-para-dioxins (PCDD) and polychlorinated dibenzo furans (PCDF), dioxin-like (dl) PCBs (non-ortho and mono-ortho substituted PCBs).

^bFor exposure estimates, data for fish oil and cod liver oil were combined and a weighted mean were used.

Table 7.1.3.3-4 Exposure to dioxins and dioxin-like PCBs from fish oil in consumers only (Norkost 3, n=663)

Food item	Lower bound Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week		Upper bound Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week	
	Mean	P95	Mean	P95
Fish oil and cod liver oil^b, n=663	0.2	0.3	0.6	1.1

P95: 95th percentiles.

^aDioxins = polychlorinated dibenzo-para-dioxins (PCDD) and polychlorinated dibenzo furans (PCDF), dioxin-like (dl) PCBs (non-ortho and mono-ortho substituted PCBs). ^bFor exposure estimates, data for fish oil and cod liver oil were combined and a weighted mean were used.

7.1.3.4 Pregnant women

Mercury

Exposure to mercury from fish in pregnant women is shown in Table 7.1.3.4-1. The mean exposure was 0.17 µg/kg bw/week, whereas 95th - and 97.5th percentile exposure was 0.39 and 0.45 µg/kg bw/week, respectively. Lean fish contributed with 82% of the mean exposure, and cod, saithe and haddock were the main sources of mercury among the lean species. This reflects merely the high consumption of cod, since the concentration of Hg in cod is not particularly high compared to less consumed species (Table 6.2-1). The median intake was 0.15 µg Hg/kg bw/week, which is more or less equal to the mean intake. The 95th percentile exposure was 2.3-fold higher than the mean exposure. The 97.5th percentile exposure for total fish was 0.45 µg/kg bw/week, for lean fish 0.40 µg/kg bw/week, for fatty fish 0.12 µg/kg bw/week and for cod roe and liver 0.01 µg/kg bw/week (not shown in Table 7.1.3.4-1).

Very few pregnant women reported to have eaten pike and perch (Tables 3.2.3-1 and 3.2.3-2), and although these species may contain higher mercury levels than other more commonly eaten species, they contributed little to exposure even at high percentiles of mercury exposure.

Table 7.1.3.4-1 Exposure to mercury from fish in pregnant women (MoBa, n= 83782)

Food item	Lower bound µg Hg/kg bw/week			Upper bound µg Hg/kg bw/week		
	Mean	Median	P95	Mean	Median	P95
Fish, total, n= 83782	0.17	0.15	0.38	0.17	0.15	0.39
Lean fish (≤5% fat)	0.14	0.13	0.34	0.14	0.13	0.34
Cod, saithe, haddock	0.12	0.10	0.29	0.12	0.10	0.28
Redfish, catfish	0.01	0 ^a	0.06	0.01	0 ^a	0.06
Pike, perch	<0.01	0 ^a	0	<0.01	0 ^a	0
Tuna	0.01	0 ^a	0.06	0.01	0 ^a	0.06
Halibut, flatfish	0.01	0 ^a	0.03	0.01	0 ^a	0.03
Fatty fish (>5% fat)	0.02	0.01	0.09	0.02	0.01	0.08
Mackerel, herring	0.02	0.01	0.07	0.02	0.01	0.07
Salmon, trout	0.01	0.01	0.02	0.01	0.01	0.02
Fish roe and liver	<0.01	0^a	<0.01	<0.01	0^a	0.01
Cod roe	<0.01	0 ^a	<0.01	<0.01	0 ^a	0.01
Cod roe and liver pate	<0.01	0 ^a	<0.01	<0.01	0 ^a	<0.01
Cod liver	<0.01	0 ^a	<0.01	<0.01	0 ^a	<0.01

^aMedian was zero because less than 50% of the participants had consumed the fish/fish product.
P95 = 95th percentile.

Dioxins and dl-PCBs

Calculated exposure to dioxins and dl-PCBs in pregnant women is shown in Table 7.1.3.4-2. The mean lower bound exposure was 0.75 pg TEQ/kg bw/week, whereas the mean UB exposure was 0.94 pg TEQ/kg bw/week. The 95th percentile exposure was at LB 2.2 pg TEQ/kg bw/week and at UB 2.7 pg TEQ/kg bw/week. Fatty fish was the main source, contributing 66% of the exposure from fish. Farmed salmon contributed 28% of the mean exposure from fish. Cod liver was eaten by few pregnant women, but contributed 23% of the mean exposure from fish. This is caused by a high contribution in women that consume cod liver in the form of bread spread (cod roe and liver pate), as can be seen at the high percentiles. The UB 97.5th percentile exposure was 3.7 pg TEQ/kg bw/week from total fish, 0.39 pg TEQ/kg bw/week from lean fish, 2.8 pg TEQ/kg bw/week from fatty fish and 1.3 pg TEQ/kg bw/week from cod roe and liver (not indicated in Table 7.1.3.4-2).

Table 7.1.3.4-2 Exposure to dioxins and dl-PCBs from fish from fish in all pregnant women (MoBa, n=83782)

Food item	Lower bound Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week			Upper bound Sum dioxins and dl-PCBs ^a pg TEQ/kg bw/week		
	Mean	Median	P95	Mean	Median	P95
Fish, total (n=83782)	0.75	0.46	2.2	0.94	0.59	2.7
Lean fish (≤5% fat)	0.085	0.062	0.24	0.12	0.097	0.32
Cod, saithe, haddock	0.055	0.047	0.13	0.088	0.075	0.21
Redfish, catfish	0.005	0 ^c	0.026	0.008	0 ^c	0.041
Pike, perch	<0.001	0 ^c	0	<0.001	0 ^c	0
Tuna	<0.001	0 ^c	0	<0.001	0 ^c	0
Halibut, flatfish	0.025	0 ^c	0.15	0.026	0 ^c	0.16
Fatty fish (>5% fat)	0.49	0.32	1.6	0.65	0.42	2.1
Mackerel, herring	0.28	0.11	1.2	0.39	0.15	1.7
Salmon, trout ^b	0.21	0.16	0.64	0.26	0.20	0.80
Fish roe and liver	0.17	0^c	0.47	0.17	0^c	0.47
Cod roe	0.032	0 ^c	0.17	0.032	0 ^c	0.17
Cod roe and liver pate	0.13	0 ^c	0	0.13	0 ^c	0
Cod liver	0.014	0 ^c	0	0.014	0 ^c	0

P95 = 95th percentile.

^aDioxins = polychlorinated dibenzo-para-dioxins (PCDD) and polychlorinated dibenzo furans (PCDF), dioxin-like (dl) PCBs (non-ortho and mono-ortho substituted PCBs).

^bFarmed salmon represents salmon and trout.

^cMedian was zero because less than 50% of the participants had consumed the fish/fish product.

Exposure from fish oil and cod liver oil in pregnant women

Exposure from fish oil and cod liver oil has not been calculated for pregnant women in the present opinion. However, a high proportion of pregnant women are consumers of fish oil and cod liver oil (77% in 2008, Chapter 3.2.3).

Daily consumption of 5 ml fish oil or cod liver oil with a mean LB (UB) concentration of 0.27 (0.95) pg TEQ/g, would correspond to an exposure to dioxins and dl-PCBs of 0.13 (LB) to

0.45 (UB) $\mu\text{g TEQ/kg bw/week}$ in pregnant women with mean pre-pregnancy body weight of 67 kg.

7.1.4 Summary of current contaminant exposure from food consumption surveys

Methylmercury exposure

For methylmercury exposure, fish is the only notable source. Methylmercury constitutes 80-100% of the total mercury in fish. The main source is lean fish (Figure 7.1.4-1).

The updated exposure assessments indicated mean and 95th percentile exposure in **2-year-olds** at 0.51 and 1.1 $\mu\text{g/kg bw/week}$. In **adults** the mean and 95th percentile exposures were 0.30 and 1.2 $\mu\text{g/kg bw/week}$, and in **pregnant women** the mean and 95th percentile exposures were 0.17 and 0.39 $\mu\text{g/kg bw/week}$, respectively. For mercury exposure from fish, the upper and lower bounds are quite similar.

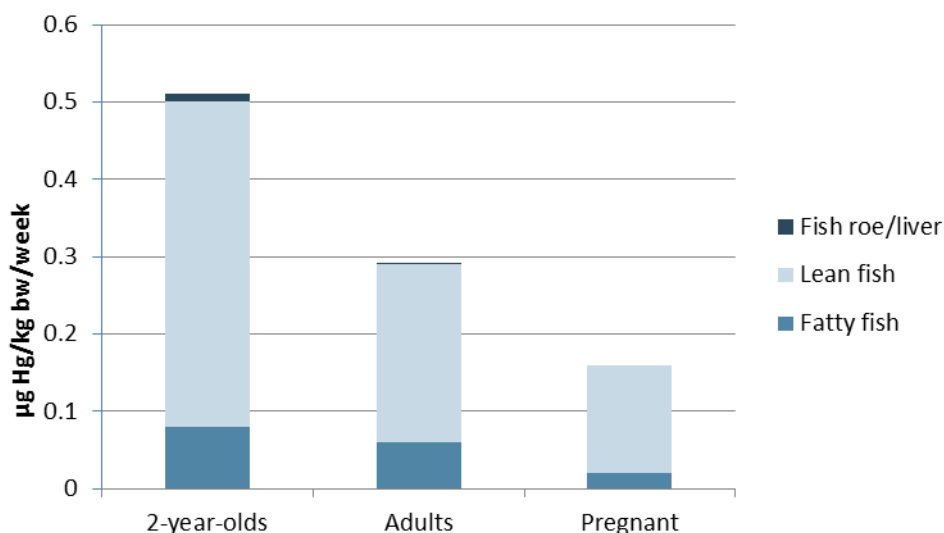


Figure 7.1.4-1 Mean upper bound (UB) exposure to mercury from fish in Norwegian 2-year-olds (småbarnskost), adults (Norkost 3) and in pregnant women (MoBa). For mercury exposure from fish, the upper and lower bounds are quite similar. Fish is grouped into fatty fish and lean fish, and fish roe and liver.

Dioxins and dl-PCBs

The updated exposure assessments from fish indicated mean exposure in **2-year-olds** between 2.0 (LB) and 2.6 (UB) and 95th percentile exposure between 7.3 (LB) and 9.4 (UB) pg TEQ/kg bw/week . In **adults** the mean exposure was between 1.4 (LB) and 1.7 (UB) pg TEQ/kg bw/week , and the 95th percentile exposure was between 5.6 (LB) and 6.8 (UB) pg TEQ/kg bw/week . In **pregnant women** the mean exposure was between 0.75 (LB) and 0.94

(UB) pg TEQ/kg bw/week and the 95th percentile exposure was between 2.2 (LB) and 2.7 (UB) pg TEQ/kg bw/week.

Fatty fish was the major contributor (Figure 7.1.4-2), but consumption of cod liver oil may contribute in addition. In adults, cod liver oil contributed a smaller part, whereas cod liver oil constitutes a larger part in 2-year-olds.

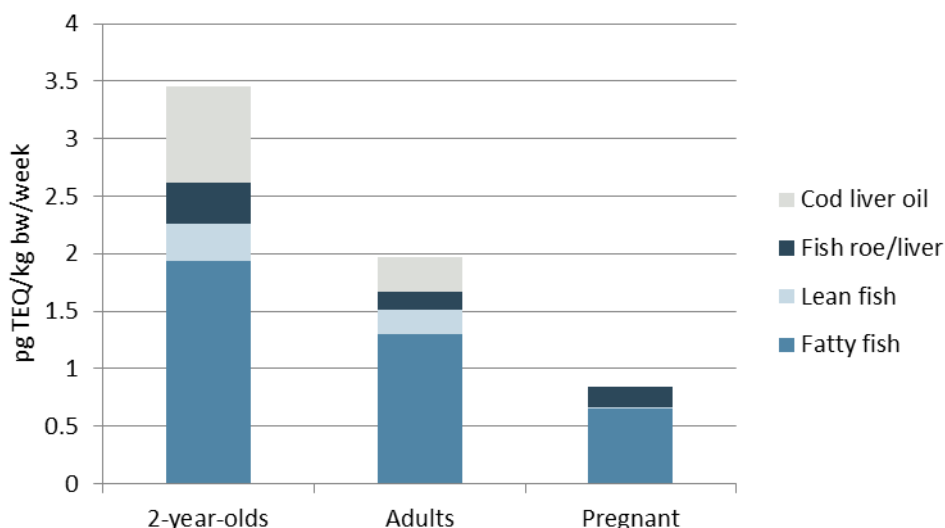


Figure 7.1.4-2 Mean upper bound (UB) exposure to dioxins and dl-PCBs from fish and cod liver oil (including fish oil) in Norwegian 2-year-olds (Småbarnskost 2007), adults (Norkost 3) and in pregnant women (MoBa, not including cod liver oil). Fish is grouped into fatty fish, lean fish and liver/roe.

7.2 Previous dietary estimates and changes in nutrient intake and contaminant exposure from fish since 2006

As summarised in Chapter 3.4, the fish consumption is largely unchanged between the VKM opinion in 2006 and the present assessment. The methods used for intake and exposure assessment particularly in adults in 2006 and in the present report are however not directly comparable and any differences between intakes of nutrients and contaminants need to be interpreted with caution. The mean is however to some extent comparable between the surveys because of the large number of participants. Data from the food consumption surveys for 2-year-olds from 2006 (Småbarnskost 1998) and the present assessment (Småbarnskost 2007) are comparable as the same method was used in both these surveys (semi-quantitative food frequency questionnaire). For both 2-year-olds, pregnant women and adults, lean fish contributes with about 60 percent of the total fish consumption, while fatty fish contributes with about 40 percent, which is more or less similar as in 2006 given the methodological differences (Chapter 3.3).

7.2.1 Eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA)

In the (VKM, 2006) fish contributed on average 200 mg EPA+DPA+DHA per day in 2-year-olds, the median was 100 mg and high consumption (95th percentile) was 700 mg/day. Use of supplements contributed on average 400 mg/day. Compared to (VKM, 2006), the amount of EPA+DPA+DHA (mg/d) from both mean and high fish consumption (95th percentile) in **2-year-olds** is unchanged, providing 200 mg and 700 mg EPA+DPA+DHA per day, respectively.

No quantitative assessment of EPA+DPA+DHA contributed by fish was given for **pregnant women** in (VKM, 2006). However, in 40108 women recruited during years the 2002 to 2005, fish oil and cod liver oil supplements were used by 59%, which will contribute substantially to the intake of these fatty acids (Chapter 3.2.3).

In 2006, in the adults, fish contributed on average 500 mg EPA+DPA+DHA, the median was 300 mg and high consumption (95th percentile) was 1300 mg/day (VKM, 2006). Use of supplements contributed on average 300 mg/day. The amount of EPA+DPA+DHA mg per day from mean total fish intake is unchanged also in **adults**, providing 500 mg EPA+DPA+DHA per day.

In 2006, the average contribution of EPA+DPA+DHA from dietary supplements was not estimated. In the current update, the average contribution of EPA+DPA+DHA from fish oil and cod liver oil supplements for **adults** was 735 and for **2-year-olds** 454 mg/day.

7.2.2 Vitamin D

In (VKM, 2006), it was estimated that fish contributed on average with 0.50 µg vitamin D per day in the **2-year-olds** and up to 1.9 µg/day for high consumers (95th percentile). In the current update, fish contributed on average 0.36 µg vitamin D per day, and high consumption contributed 1.32 µg/day. There has been a modest decline in estimated vitamin D contributed by fish in 2-year-olds.

The contribution from fish to vitamin D intake in **adults** was in (VKM, 2006) estimated to be on average 2.6 µg vitamin D per day. The current estimated average contribution from fish in adults is 2.1 µg vitamin D per day. In 2006, the average contribution of vitamin D from dietary supplements for adults was 5.9 µg/day. In the current update, the average contribution of vitamin D from fish oil and cod liver oil supplements for adults was 3.5 µg/day. Since 2006, vitamin D contributed by fish has been calculated and published in the Fish and Game Study, part C. In 101 men and women who did not consume fish liver, the median intake of vitamin D from fish was 2.2 µg/day, which is comparable to the current estimate in adults (Birgisdottir et al., 2012).

In (VKM, 2006) estimated vitamin D contributed by fish in **pregnant women** was not reported. In a study in 40108 MoBa participants recruited during years 2002 to 2005, fish oil

and cod liver oil supplements were used by 59%, which contributed substantially to the intake of vitamin D (Haugen et al., 2009).

7.2.3 Iodine

(VKM, 2006) did not report the contribution of iodine from fish in **2-year-olds** or **pregnant women**. In scenarios in **adults** with low (27 g/day), median (65 g/day) and high consumption of "fish and other seafood" (119 g/day) and a distribution with 2/3 lean and 1/3 fatty fish, iodine contributed by the three different scenario intakes were estimated to be 76, 180 or 340 µg/day.

The updated mean estimate of iodine in **adults** is 86 µg iodine per day, which is apparently lower than the scenario based on median fish consumption in 2006. The reason for this difference is not fully known, but the iodine data in the present exposure assessment is based on levels in different fish species as described in Chapter 6, whereas the iodine levels used for exposure assessment in the scenario from 2006 are described as a range for different species, and the exact figures used were not given. There is no environmental or biological reason why iodine intake from fish should be decreased since 2006 as long as the fish consumption is unchanged, and the discrepancy may be explained by a better database and thus less uncertainty in the exposure assessment than in 2006.

7.2.4 Selenium

(VKM, 2006) did not report the contribution of selenium from fish in **2-year-olds** or **pregnant women**. In **adults**, selenium contributed by fish was estimated in the same scenario as described above for iodine. Low, median and high fish consumption with 2/3 lean and 1/3 fatty fish contributed 9, 22 and 41 µg selenium per day in 2006.

In the current update, average adult fish consumption contributed 15 µg selenium per day, which is apparently lower than that at the scenario at median fish consumption in 2006. As for iodine, the reason for the difference is not fully known. The selenium data in the present exposure assessment is based on levels in different fish species as described in Chapter 6, whereas the selenium levels used for exposure assessment in the scenario from 2006 generally were slightly higher in the different fish species.

7.2.5 Mercury

The main difference regarding mercury exposure from fish is that the database on mercury concentrations in fish has been substantially improved since the VKM assessment in 2006, and this has reduced the uncertainty in the exposure estimates.

The mercury exposure from fish in **2-year-olds** was at median 0.3 µg/kg bw/week (95th percentile 0.8 µg/kg bw/week) in 2006, and the exposure in the present opinion is at UB median 0.45 µg/kg bw/week (mean and 95th percentile of 0.51 and 1.16 µg/kg bw/week).

The median exposure to mercury from fish and other seafood was in **adults** in 2006 estimated to 0.4 µg/kg bw/week, whereas the mean adult exposure in the present opinion based on Norkost 3 is 0.3 µg/kg bw/week, and in **pregnant women** in MoBa 0.17 µg/kg bw/week in the present opinion. The lower exposure in pregnant women than in adults can be explained by lower fish consumption among pregnant women than in the general population, in addition to different dietary recall methods.

There are no good time-trend data on mercury levels in fish however, the data do not indicate a reduction in mercury levels in fish. The exposure data indicate an increase in children, while differences in dietary methods prevent conclusions on differences in exposure levels in adults.

Since publication of the VKM report in 2006 (VKM, 2006), two studies on dietary exposure to mercury have been published in Norway, as summarised below. For these two publications, the database used for exposure assessment in (VKM, 2006) was extended and improved.

Total mercury exposure from fish and other food was calculated in the Norwegian Fish and Game study part C (n=184) based on the FFQ in the study and an extensive database on levels in food in Norway, covering the total diet. The median mercury exposure was 0.3 and 0.4 µg/kg bw/week in a group of adult consumers considered representative for The Fish- and Game study part B (which was representative for selected counties in Norway) and in a group including high fish consumers, respectively. Seafood contributed to 95% of the exposure. A commonly used toxicokinetic model indicated that the dietary intake exposure estimate moderately underestimated the measured mercury in blood among participants with the highest blood mercury level (Jenssen et al., 2012).

Total mercury exposure from fish and other food has also been calculated for participants in MoBa (n=62 941), based on the same database as in (Jenssen et al., 2012). Median exposure to Hg was 0.15 µg/kg bw/week (P5-P95: 0.03-0.38). The mean contribution from seafood consumption was 88% of total mercury exposure (Vejrup et al., 2014).

Both the abovementioned studies report mercury exposure quite similar as found in the present exposure assessment in adults and pregnant women.

7.2.6 Dioxins and PCBs

Also for dioxins and dl-PCBs the database on concentrations in fish has improved substantially since the assessment in 2006, reducing the uncertainty in the exposure assessments. There is a decreasing trend of dioxins and dl-PCBs in humans, indicating decreasing exposure (VKM, 2013a). Since food is a major source, this means that the levels in food are decreasing, although there are no trend data in food in Norway available to show this decrease.

In **adults**, the median UB intake of dioxins and dl-PCBs from fish and other seafood was estimated to be 4.7 pg TEQ/kg bw/week in 2006, and in the present opinion the mean UB

exposure was 1.7 pg TEQ/kg bw/week (LB 1.4 pg TEQ/kg bw/week). The mean exposure from fish in adults in 2014 is thus substantially lower, approximately 36% of what was calculated in 2006.

In the present opinion the mean UB exposure from fish in **pregnant women** (MoBa) was 0.94 pg TEQ/kg bw/week (LB 0.75), which is lower than the mean in adults (Norkost 3). The lower exposure in MoBa than in adults in Norkost 3 can be explained by lower fish consumption among pregnant women than in the general population, in addition to different dietary recall methods.

Exposure in children at **2-years-olds** was only shown in figures in (VKM, 2006), and no numerical data were given. Exposure in **pregnant women** was not shown.

Since publication of the VKM report in 2006 (VKM, 2006), two studies on dietary exposure to dioxin and dl-PCBs have been published in Norway, as summarised below. For these two publications, the database used for exposure assessment in the VKM report (VKM, 2006) was extended and improved.

In the Norwegian Fish- and Game study part C (conducted in 2003), 73 representative consumers and 111 high consumers of fish and game filled in a food-frequency questionnaire (FFQ) that covered the entire diet. The food consumption data were coupled to an extensive database on levels of dioxins and dl-PCBs in food in Norway in the period 2000-2006. The estimated median intakes (LB) of dioxins and dl PCBs were 5.46 and 8.75 pg TEQ/kg bw/week in two groups of consumers with different seafood consumption, respectively. In these groups, fish and other seafood contributed with 70 and 71% of the exposure, respectively (Kvalem et al., 2009).

The same database on levels of dioxins and dl-PCBs in food as the one used in (Kvalem et al., 2009) has been used to calculate the intake of dioxins and dl-PCBs and PCB-153 in participants in the MoBa cohort between 2002 and 2009 (83524 participants). The mean (median) LB intake of dioxins and dl-PCBs was 4.73 (3.56) pg TEQ/kg bw/week (Caspersen et al., 2013). Fish and other seafood contributed with 41% of the exposure, corresponding to 1.95 pg TEQ/kg bw/week (personal communication, IH Caspersen).

Based on the above, it can be concluded that the mean exposure from fish in **pregnant women** based on the database of levels of dioxins and dl-PCBs in fish in the present opinion (Chapter 5.5.1) is approximately 40% of the level calculated based on the previous database, which contained fish analysed in the period 2000 to 2006. The decrease is likely due to a combination of more accurate data on levels in fish, which reduces the uncertainty, and decreased levels of dioxins and dl-PCBs in the environment.

7.2.7 Summary of changes in nutrient intake and contaminant exposure since the benefit-risk assessment in 2006

The updated **nutrient** calculations in the current opinion indicate no change in EPA+DPA+DHA contributed by fish consumption, a modest decline in the amount of vitamin D contributed by fish, and a substantial decline in iodine and selenium. There is no environmental or biological reason why iodine and selenium intake from fish should be decreased since 2006, as long as the fish consumption is unchanged. The observed differences may be explained by better databases and thus less uncertainty now than in the exposure assessments in 2006.

The main difference regarding **mercury** exposure from fish is that the database on mercury concentrations in fish has been substantially improved since the assessment in 2006, and this has reduced the uncertainties in the exposure estimates. Overall, the exposure estimates for mercury from fish in 2006 and 2014 are quite similar.

Also for **dioxins and dl-PCBs** the database on concentrations in fish has improved substantially since the assessment in 2006, reducing the uncertainty in the exposure assessments.

There is a decreasing trend of dioxins and dl-PCBs in the environment and therefore also in food. A decrease in exposure to dioxins and dl-PCBs from fish can be seen since 2006, as present exposure is estimated to be in the range of 40% of the exposure calculated in 2006. The decrease is likely due to a combination of more data on levels of dioxins and dl-PCBs in fish in 2014 than in 2006, and decreased levels of dioxins and dl-PCBs in the environment.

VKM has made various scenarios to foresee how possible changes in fish consumption pattern and amounts will affect the contribution from fish to the recommended intakes of specific important nutrients, as well as to exposure to tolerable weekly intakes (TWI) of mercury, dioxins and dl-PCBs, see Chapter 8.

8 Benefit and risk characterisation of fish consumption

8.1 Background

Fish is an important component of a varied diet for the Norwegian population-at-large, providing a number of nutrients that are important for achieving a balanced diet for children, adults and the elderly. The nutritional benefits of fish consumption have long been recognised by health authorities in Norway and many other countries. Thus, in 2006, the Norwegian recommendation for fish consumption was to eat more fish both for dinner and as bread spread. In 2014, based on the VKM assessment in 2006 (VKM, 2006) and the report "Dietary advice to promote public health and prevent chronic diseases in Norway" (Norwegian National Council for Nutrition, 2011), these recommendations were altered and made quantitative by the Norwegian Directorate of Health (2014). The current recommendation is to eat fish as dinner meals 2-3 times per week for all age groups, representing 300-450 g fish per week for adults, including at least 200 g fatty fish such as salmon, trout, mackerel and herring. Fish is also recommended as bread spread. A further exception is given for young females and pregnant women, who should, over time, avoid eating more than the equivalent to two meals of fatty fish per week, including fish like salmon, trout, mackerel and herring (Chapter 1). The Norwegian health authorities also recommend a daily supplement of vitamin D to infants from 4 weeks of age, and if this supplement is taken as cod liver oil it will in addition ensure an adequate supply of n-3 LCPUFAs.

Norwegians have traditionally had a relatively high fish and seafood consumption, especially in the coastal areas. Furthermore, fishing and hobby angling contribute to higher fish consumption in subgroups of the population. During the last decade farmed Atlantic salmon and to some extent also farmed rainbow trout, have become important food items in the Norwegian diet. Norway is globally one of the largest producers of farmed Atlantic salmon and rainbow trout (Chapter 5).

Fish, as other food, contain both beneficial (i.e. nutrients) and potential hazardous compounds (i.e. contaminants), and the weighing of benefits and risks of food/fish consumption has become a main public health issue. For some decades, concerns about potential risks associated with exposure to contaminants from food have resulted in strong focus on chemical management and policy both nationally and internationally. Stricter controls, use-restrictions and bans of the most hazardous contaminants, have resulted in a significant decline in concentrations the last 20 years, both in the environment and in humans (Chapter 2).

In 2006, VKM published a benefit-risk assessment of fish in the Norwegian diet (VKM, 2006). At that time, there was little experience with benefit-risk assessment. For the benefit assessment VKM therefore mirrored the risk assessment paradigm that was well established (hazard identification and characterization (including dose-response assessment), exposure assessment and risk characterisation). Thus, the beneficial effect of fish was assessed by the following four steps; positive health effect identification, positive health effect characterisation (dose-response assessment), exposure assessment and benefit characterization. In the final benefit-risk assessment a comparison of the benefits and risks was done (VKM, 2006).

A similar approach is recommended by EFSA (2010a) in the Opinion "Guidance on human health risk-benefit assessment of foods". Furthermore, a stepwise approach; i) initial assessment, addressing the question whether the health risks clearly outweigh the health benefits or vice versa, ii) refined assessment, aiming at providing semi-quantitative or quantitative estimates of risks and benefits at relevant exposure by using common metrics, and iii) comparison of risks and benefits using a composite metric such as disability-adjusted life year (DALY) or quality-adjusted life year (QALY) to express the outcome of the risk-benefit assessment as a single net health impact value is recommended. In the same opinion EFSA also emphasizes the importance to discuss strength and weaknesses of the data sets used in the different steps as well as its associated uncertainties.

The present benefit-risk assessment is comprised of three elements, i.e. benefit assessment, risk assessment and benefit-risk comparison. This methodology is in accordance with EFSA EFSA (2010a) for steps i) - ii). To estimate the effect of fish consumption on disability-adjusted life year (DALY) or quality-adjusted life year (QALY) to express the outcome of the risk-benefit assessment as a single net health impact value for the Norwegian population was not considered necessary based on the outcomes of the first two steps. Uncertainties are addressed in Chapter 9.

8.2 Fish consumption in Norway

On an average, Norwegians eat more fish than most other Europeans (except Spaniards and Italians) (EFSA, 2014b). In this assessment, VKM has used information about fish consumption from more recent national dietary surveys among 2-year-olds (Kristiansen et al., 2009) and adults (18-70 years of age, (Totland et al., 2012) as well as information for pregnant women who answered the Norwegian Mother and Child Cohort Study (MoBa) food-frequency questionnaire (FFQ) (Brantsaeter et al., 2008; Magnus et al., 2006; Meltzer et al., 2008).

The distribution in terms of portions depends on the portion sizes of dinners and amount of spread used on bread. (VKM, 2006) defined a dinner portion as 200 g and a portion of fish spread as 25 g. The national food-based dietary guidelines for total fish consumption (Norwegian Directorate of Health, 2014) could be met by two fish dinners and two slices of

bread with fish spread weekly. When a smaller dinner portion is used, e.g. 150 g as used in this report, two fish dinners and fish spread on six bread slices weekly is needed to meet the recommendation.

In 2006, dietary intakes of fish by the age groups 4-, 9-, and 13-year-olds were estimated from the national food consumption survey Ungkost 2000 (VKM, 2006). These food consumption data are considered too old to be used in this opinion. Thus, fish consumption by these particular age groups has not been assessed in the present report, and it is therefore not known if the fish consumption patterns have changed, neither in amount consumed nor type of fish eaten for these age groups (Chapter 3.3).

Fish consumption per week of the different age groups is summarised in the table Table 8.2-1.

Table 8.2-1 Fish consumption (expressed as raw fish), mean grams (g) per week in 2-year-olds (Småbarnskost 2007, n=1674), adults (Norkost 3, n=1787) and pregnant women (MoBa, n=86277)

Population groups	Mean fish consumption g/week			Fish roe and liver
	Fish, total	Lean fish, cod (\leq 5% fat)	Fatty fish ($>$ 5% fat)	
2-year-olds	112	70	35	7
Adults	364	210	147	7
Pregnant women	217	126	77	14

Adults eat on average 364 g/week (equivalent to 2-3 fish dinner servings per week given a portion size of 150 g), pregnant women eat 217 g per week (equivalent to 1-2 dinner servings per week given a portion size of 150 g), while 2-year-olds eat 112 g/week (equivalent to 1-2 dinner servings per week given a portion size of 75 g).

Approximately sixty percent of the consumption consists of lean fish and minced fish products. Pregnant women eat fatty fish in amounts equivalent to half a dinner serving per week. For all age groups Atlantic cod is the most eaten lean fish species, and for pregnant women mackerel and farmed Atlantic salmon are equally important fatty fish species (on average 42 g mackerel versus 35 g farmed salmon per week), while for adults farmed salmon is more important than mackerel as a fatty fish species consumed (on average 84 g farmed salmon versus 28 g mackerel per week). For 2-year-olds, mackerel is the most eaten fatty fish species (on average 21 g mackerel versus 7 g farmed salmon per week). For details on fish consumption in Norway, see Chapter 3.

8.2.1 Comparison of fish consumption; 2014 versus 2006

Pregnant women and 2-year-olds: Although the methods used to assess fish consumption in this assessment are not directly comparable with the respective methods used by VKM in 2006 (Chapter 3.3), the fish consumption (g/week) does not appear to have

changed substantially since 2006 for 2-year-olds and young women (represented as pregnant women in the present report).

Adults: For adults, the methods used for assessment of fish consumption differ substantially between 2006 and 2014 (Chapter 3.3), however a rough comparison of mean intake does indicate fish consumption in the same order of magnitude.

For both 2-year-olds, adults and pregnant women, lean fish contributes with about 60 percent of the total fish consumption, while fatty fish contributes with about 40 percent, which is similar as to 2006 given the methodological differences (Chapter 3.3).

8.2.2 Comparison of fish consumption in Norway with food based dietary guidelines

The Norwegian Directorate of Health (per 2014) recommends fish as dinner meal 2-3 times per week for **all age** groups. Fish is also recommended as bread spread. This recommendation represents totally 300-450 g fish per week for adults, and less for children due to smaller portion size. For adults, at least 200 g should be fatty fish such as salmon, trout, mackerel and herring (Chapter 1).

Two-year-olds: There are no specific dietary guidelines for fish intake for 2-years-olds, however, the Norwegian Directorate for Health recommends (per 2014) fish as dinner meal 2-3 times per week for **all age** groups. The average fish intake (112 g fish per week) is about one third of adult intake equivalent to approximately one and a half dinner serving per week.

Adults: The average fish intake (364 g/week) reaches the recommended intake of total fish consumption (300-450 g fish/week), but the average intake of fatty fish (147 g/week) does not reach the recommendation for fatty fish consumption (200 g/week).

Pregnant women: The average fish intake (217 g/week) does not reach the recommended intake of total fish consumption (300-450 g/week). The average intake of fatty fish (77 g/week) is about 1/3 of the recommended intake of fatty fish (200 g/week). However, high fish consumers (95th percentile: 476 g/week, which refers to approximately three dinner servings per week) do reach the recommended intake of total fish consumption. Furthermore, the high intake of fatty fish (95th percentile: 252 g/week) reaches the recommended intake of at least 200 g fatty fish per week. A study in a subset of the same population of pregnant women found that only 23% of the women reached the recommended intake of 300-450 g fish per week, and only 6.7% reached the recommended intake of at least 200 g fatty fish per week (von Ruesten et al., 2014).

VKM concludes that of the different population groups, only adults (18-70 years of age) with an average or higher fish consumption reach the food based dietary guidelines for total fish consumption (Norwegian Directorate of Health, 2014). Both the mean total and fatty fish consumption in children (2-year-olds) and

pregnant women as well as the mean fatty fish consumption in adults are lower than recommended. Pregnant women especially have too low fish consumption to meet the dietary guidelines.

8.3 Health effects of fish consumption

Epidemiological studies can demonstrate statistically significant associations between dietary exposures and health outcomes. However, because of all the other exposures occurring simultaneously in the complex lives of humans that can never be completely accounted for, such studies cannot provide evidence of cause and effect. Only randomized controlled trials have a study design that can demonstrate causal effects in humans. Such trials are however not feasible for long-term dietary exposure. Therefore, evidence from observational studies of dietary exposures and disease outcomes are necessary and important. When sufficient studies exist, in diverse settings and with adequate elimination of random error, systematic error (bias), and logical error (confounding), then the causal nature of observed associations can be reasonably assessed. The evidence contributed by observational epidemiological studies is inversely related to the degree of uncertainty. For more details regarding general limitations and uncertainties in interpretation of data from epidemiological studies, see Chapter 9.3.

Fish contain both beneficial components (e.g. nutrients like n-3 LCPUFA and vitamin D) and possible hazardous compounds (e.g. methylmercury, dioxins and PCBs). Very few studies have examined the influence of beneficial effects of fish, taking into account the contaminants present. When balancing the benefits of fish consumption on a specific health outcome, i.e. cardiovascular disease and optimal neurodevelopment, with the risk from contaminants such as PCBs, dioxins and methylmercury in fish, the net outcome may be affected by the degree of contaminant exposure. Thus, “negative confounding”, which denotes that two opposing forces coexist in the same food and influence the outcome in opposite directions is a particular challenge when conducting and evaluating studies of fish consumption (Stern and Korn, 2011). For a comprehensive summary of health effects associated with fish consumption, see Chapter 4.8.

8.3.1 Epidemiological studies addressing fish consumption and different health outcomes

In VKM (2006), possible health effects associated with fish consumption was assessed by reviewing relevant available epidemiological data on associations between fish consumption and the health outcomes cardiovascular disease, cancer, growth and development of foetus and infant, and allergy to fish and other seafood. The data sources were quite limited. Since then, several extensive observational studies and intervention studies have been conducted, addressing beneficial effects of fish and EPA+ DHA supplementation on specific health outcomes in the general population and/or specific subgroups. Thus, since 2006, the

knowledge-base for assessing health effects associated with fish consumption is considerably strengthened.

In the present VKM report, the literature reviewed (Chapter 4) addressing fish consumption and effects on specific health outcomes that was considered relevant for the benefit-risk evaluation includes systematic reviews and meta-analyses, assessments prepared by international scientific bodies as well as some single cohort or population-based studies published after 2006, (see Chapter 4.1 for details with regards to strategy for selection of epidemiological studies assessed). It appears that of the health endpoints assessed, there are more studies and more evidence related to fish consumption and cardiovascular endpoints and neurodevelopment than for the other endpoints assessed in this up-date (cancer; type-2 diabetes and other metabolic outcomes; asthma, allergy, and other atopic diseases; pregnancy related outcomes; neurodevelopment; and cognitive decline including Alzheimers disease).

Criteria for objectively evaluating the level of causality of associations observed in epidemiology were stated by Hill (1965). These criteria, which include consistency and strength of the association, dose-response, time order, specificity, consistency on replication, predictive performance, biological plausibility and coherence, must be applied when discussing the results observed in every study. For characterisation of a possible beneficial health effect of fish consumption, a dose-response assessment is a prerequisite.

VKM has summarized research on association between fish consumption and several health effects (cardiac disease, neurodevelopment and other outcomes related to the central nervous system, cancer, type-2 diabetes and other metabolic outcomes, asthma, allergy and other atopic outcomes, and pregnancy related outcomes). A comprehensive summary of health effects associated with fish consumption is given in Chapter 4.8.

VKM concludes that meta-analyses conducted since 2009 do not show association between fish consumption and **cancer**. Furthermore, the studies summarized have not revealed consistent associations between fish consumption and **type-2 diabetes**, although some Nordic studies indicate protective associations. None of the studies controlled for contaminant exposure from fish, and it is not known whether this would have affected the outcome.

No studies reported association between fish consumption and adverse health effects. A few studies showing positive health effects of fish consumption reported negative confounding by contaminants in fish.

8.3.2 Fish consumption in Norway and beneficial health effects

For **pregnancy-related outcomes**, results from MoBa indicate that fish consumption during pregnancy, and in particular lean fish consumption, is associated with **increased birth weight and lower risk of preterm birth**. Studies also indicate that prenatal exposure to both mercury and dioxins and PCBs can decrease birth weight. VKM concludes

that this implies that the overall beneficial effect of fish consumption on birth weight might have been more beneficial in the absence of contaminants, and that the findings need to be confirmed in other cohorts.

Regarding **atopic diseases**, VKM noted that the studies indicate a protective association between maternal fish consumption and/or early life fish consumption and **atopic diseases**. None of the studies controlled for contaminant exposure from fish and it is not known whether this would have affected the outcome.

No dose-response assessment was possible for the abovementioned end points.

It is only for the health outcomes cardiovascular diseases and neurodevelopment that adequate data on relationships between dose (fish consumed) and response are available (Chapter 4). It should be noted that information on type of fish species constituting "fish consumption" in the epidemiological studies was generally absent. Thus, in the following a comparison is attempted of the present Norwegian fish consumption (in terms of fish servings per week or g fish per week) and the corresponding fish consumption in epidemiological studies associated with effects on cardiovascular diseases and optimal neurodevelopment.

It should be noted that servings used in different studies were not always quantified and varied considerably. The servings were generally lower than the portion sizes used in this opinion.

Cardiac mortality: VKM notes that the beneficial effect of seafood consumption on cardiac mortality is observed at relatively low fish consumption, 1-2 servings of fish per week, and up to 3-4 servings per week. Furthermore, VKM notes that the calculated benefits of fish consumption in relation to cardiac mortality refer to net effects combining beneficial, neutral, and adverse effects of nutrients and non-nutrients, including contaminants such as methylmercury, dioxins, dl-PCBs. VKM also notes that EPA and DHA play a role. However, the beneficial effects of fish intake on cardiac mortality are most likely mediated through a complex interplay among a wide range of nutrients commonly found in fish, thus fatty and/or lean fish may be involved.

Other cardiovascular outcomes: VKM notes that the beneficial effect of fish consumption on the risk of multiple other adverse cardiovascular health outcomes, including ischaemic stroke, non-fatal coronary heart disease events, congestive heart failure and atrial fibrillation being stronger among those who had moderate (2-4 fish servings per week) than those who consumed low amounts of fish (1 or less fish serving per week). A dose dependent inverse relationship between fish consumption and EPA+DHA with heart failure incidence exist; fish intake 1-4 servings per week is associated with a risk reduction of up to 15% compared to less than 1 serving of fish per week. However, the beneficial effects of fish intake on cardiovascular risk are most likely mediated through a complex interplay among a wide range of nutrients commonly found in fish, thus fatty and/or lean fish may be involved.

Norwegian fish consumption and cardiovascular disease: The average fish consumption of adult Norwegians, 364 g/week equivalent to about 2-3 fish servings per week, is within the range considered to be beneficial according to epidemiological studies, and should give significant beneficial effects on cardiovascular outcomes on a population level. The average fish consumption in pregnant women, about 200 g/week including 77 g fatty fish, is at the lower end of fish consumption that may have beneficial effect on cardiac death, while the high consumers (95th percentile) are within the range of beneficial fish consumption. Adults including pregnant women, who eat little or no fish, may miss the beneficial effects of fish consumption on cardiovascular outcomes.

VKM notes that when balancing the benefits of fish consumption on cardiovascular disease with the risk from contaminants such as PCBs, dioxins and methylmercury in fish, the net outcome is affected by the degree of contaminant exposure. Furthermore, VKM notes that it is difficult and sometimes even impossible to compare contaminant exposure between studies. However, for all age groups in Norway, both with average and high fish consumption, the exposures from fish is well below the tolerable weekly intake for methylmercury and dioxins and dl-PCBs also for the high consumers (95th percentile).

Neurodevelopmental outcomes: VKM notes that the beneficial effect of fish/seafood consumption and children's neurodevelopment is observed at relatively low fish consumption, of about 1-2 servings per week, and up to 3-4 servings per week, compared to no fish/seafood consumption. VKM also notes that the calculated benefits of fish consumption in relation to neurodevelopmental outcomes refer to fish/seafood per se, including nutrients (e.g. DHA, iodine) and contaminants (such as methylmercury, dioxins and dl-PCBs) contained in fish/seafood. Furthermore, VKM acknowledges that the observed health benefits of fish consumption during pregnancy on neurodevelopment may depend on the maternal status with regard to nutrients and the contribution from fish relative to other sources of nutrients important for neurodevelopment.

VKM notes that high prenatal methylmercury exposure due to maternal consumption of fish high in methylmercury may reduce the beneficial effect of fish consumption on neurodevelopment. VKM also notes that high exposure to dioxins and PCBs may reduce the beneficial effect of fish consumption on neurodevelopment. The tolerable weekly intakes (TWIs) of both methylmercury and dioxins and dl-PCBs, respectively, are set to protect the most vulnerable groups (unborn children and infants). VKM (present report) has calculated that for 2-year-olds, pregnant women and adults, both mean exposure and 95th percentile exposures from fish are below the TWIs for these contaminants.

Norwegian fish consumption and optimal neurodevelopment: The average fish consumption in pregnant women, about 200 g including 77 g fatty fish per week, is at the lower end of fish consumption that may have beneficial effect on neurodevelopment according to epidemiological studies. The high consumers (95th percentile) have sufficient consumption to be in the range of beneficial effect. Pregnant women, who eat little or no

fish, may miss the beneficial effects on neurodevelopmental outcomes in foetuses and infants.

VKM is of the opinion that according to epidemiological studies, the net effects of the present average fish consumption in Norway for adults including pregnant women is beneficial for specific cardiovascular diseases (particularly cardiac mortality, but also with regard to ischaemic stroke, non-fatal coronary heart disease events, congestive heart failure and atrial fibrillation) as well as for optimal neurodevelopment of foetuses and infants. VKM notes that EPA and DHA play a role however, the beneficial effects of fish consumption on these health outcomes are most likely mediated through a complex interplay. Furthermore, VKM is of the opinion that adults and pregnant women with fish consumption less than one serving per week may miss these beneficial effects. The health benefit of fish consumption is reported from 1-2 dinner servings per week and up to 3-4 dinner servings per week. For higher fish intake per week the limited number of consumers in epidemiological studies does not allow for drawing firm conclusions about the actual balance of risk and benefit at these high intakes. More knowledge is needed to reveal the beneficial mechanisms of fish consumption.

8.4 Benefit characterisation of nutrients in fish

Fish provide us with a number of nutrients. The nutrient composition, with the exception of protein, may vary between fish species and within a species depending on factors like age, reproductive and nutritional status. Fish are recognised as an important source of animal protein with balanced amino acid profile optimal for human requirement of essential amino acids. Fish species high in fat such as salmon, herring and mackerel are usually rich in n-3 LCPUFAs and lipid-soluble vitamins like vitamin D. Fish is also regarded as a valuable source of minerals and trace elements like iodine and selenium.

Based on intake estimates in comparison with upper limits of nutrients, it is unlikely that fish consumption in Norway could lead to harmful high intake of vitamins, minerals or n-3 LCPUFAs for any age group. Therefore, in the present assessment of nutrients VKM focuses on the possible benefits of intake of nutrient from fish consumption in relation to recommended nutrient intakes.

8.4.1 Comparison of nutrients in fish; 2014 versus 2006

Wild caught fish: The available database on nutrient concentrations in wild fish have been expanded somewhat since 2006, but is still generally limited and based on relatively low numbers of fish. For some wild fish species, data are lacking or the most recent data available are analysed in 2005. The databases both in 2006 and 2014 are somewhat limited for optimal trend analyses, however there seem to be minor or no changes of the composition and concentrations of nutrients in wild caught fish.

Farmed Atlantic salmon: The available database on nutrients is expanded substantially since 2006, and nutrient concentration data in farmed Atlantic salmon is the most recent available (2013). The expanded database on nutrients reduces the uncertainties in the intake estimates compared to 2006.

Since 2006, the raw materials used in feed for Norwegian farmed Atlantic salmon and trout have substantially changed (Chapter 5). Up to 70% of the fish meal and fish oil are replaced by plant proteins and vegetable oils which has resulted in a change in nutrient composition in Atlantic salmon fillet since 2006 (VKM, 2006). The changes are shown in Table 8.4.1-1.

Table 8.4.1-1 Nutrient levels in farmed Atlantic salmon used by VKM in 2006 and 2014

	EPA+DPA+DHA mg/100g	Vitamin D µg/100g	Selenium µg/100g	Iodine µg/100g	n-6 mg/100g
VKM report 2006	2700	8	30	6-34	520
VKM report 2014	1311	7.5	12	4	2300
Change 2006 to 2014	~50% reduction	unchanged	~60% reduction	unknown	~4-fold increase

VKM concludes that with regard to EPA, DPA and DHA, and selenium, the concentrations in farmed Atlantic salmon are about 50 and 40%, respectively, of the corresponding levels in 2006, while the concentration of vitamin D is unchanged. The level of iodine in farmed Atlantic salmon was low in 2006, and is still low. The level of n-6 fatty acids is about 4-fold higher than in 2006. The composition and concentrations of nutrients in wild caught fish are not substantially different in 2014 and 2006.

8.4.2 Comparison of nutrient intake estimates with recommended intakes

In the following, VKM has estimated the contribution from fish to the recommended intakes of certain nutrients (see Terms of reference). Fish is the major source of EPA+DPA+DHA, but for Vitamin D, iodine and selenium there are also other substantial sources. Fish is not a major dietary source of n-6 fatty acids. However, inclusion of plant oils in the feed for farmed Atlantic salmon has led to an increased amount of n-6 fatty acids in the fillet compared to 2006. The current average intake of n-6 fatty acids in Norwegian adults is approximately 11 g/day, i.e. 5 percentage of energy intake (E%) (Norwegian Directorate of Health, 2014). In the present report, the average daily intake of n-6 fatty acid from farmed Atlantic salmon in adult is estimated to be 0.306 g. Thus, farmed Atlantic salmon contributes with less than 3% of the daily n-6 fatty acid intake based on a total energy intake of 2000 kcal/day. The contribution of dietary n-6 fatty acids from farmed salmon compared to the overall dietary intake of n-6 fatty acids is low and will not be discussed further.

8.4.2.1 Eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA)

Norway does not have any specific EPA, DPA or DHA recommendations for adults and children, while for pregnant and breastfeeding women the recommendation from the Norwegian Directorate of Health is 200 mg DHA per day. The intake recommendations from EFSA (2010b) are used; 250 mg EPA+DHA per day for adults and 250 mg EPA+DHA plus 100 mg DHA for pregnant. For 2-year-olds, the EFSA recommendation (EFSA, 2010b) for adults is adjusted for portion size (50% of adult portion) and set to 125 mg EPA+DHA (Chapter 2.3).

Adverse effects of high intakes of EPA+DPA+DHA has not been reported, and there is no Upper level (UL) established (VKM, 2011b).

Two year olds: Fish consumption contributes on average 204 mg EPA+DPA+DHA per day and up to 696 mg day for high fish consumption (95th percentile). Thus, the average fish intake in 2-year-olds is sufficient to meet the EFSA recommendation (EFSA, 2010b) of ~125 mg/day (Chapter 2.2.1). Contribution from fish oil/cod liver oil comes in addition.

Adults: Fish consumption contributes on average with 475 mg EPA+DPA+DHA per day, thus, the average fish intake in adults is sufficient to meet the EFSA recommendation (EFSA, 2010b) of 250 mg/day (Chapter 2.3). Noteworthy, high consumption of lean fish will also contribute with EPA+DPA+DHA. Contribution from fish oil/cod liver oil comes in addition.

Pregnant women: Fish consumption contributes on average 312 mg EPA+DPA+DHA per day and up to 992 mg/day for high fish consumption (95th percentile). EPA and DPA constitute more than 20 percent of the fatty acids (i.e. EPA+DPA+DHA), thus the average total fish intake is insufficient to meet the EFSA recommendation (EFSA, 2010b), but sufficient to meet the national recommendation of DHA per day. In contrast, high consumption (95th percentile) will meet both the national and EFSA recommendations (EFSA, 2010b) for DHA. Contribution from fish oil/cod liver oil comes in addition.

In all three population groups, consumption of cod liver oil or other fish oil is common, and daily consumption in amounts as suggested on the products will contribute four times the recommended intake of EPA+DHA. Thus, a daily intake of 5 ml cod liver oil (manufacturer's recommendation) contributes in addition with a mean intake of 1280 mg EPA+DPA+DHA per day.

Comparison of intake estimates of EPA+DPA+DHA and reference values is visualised in Figure 8.4.2.1-1.

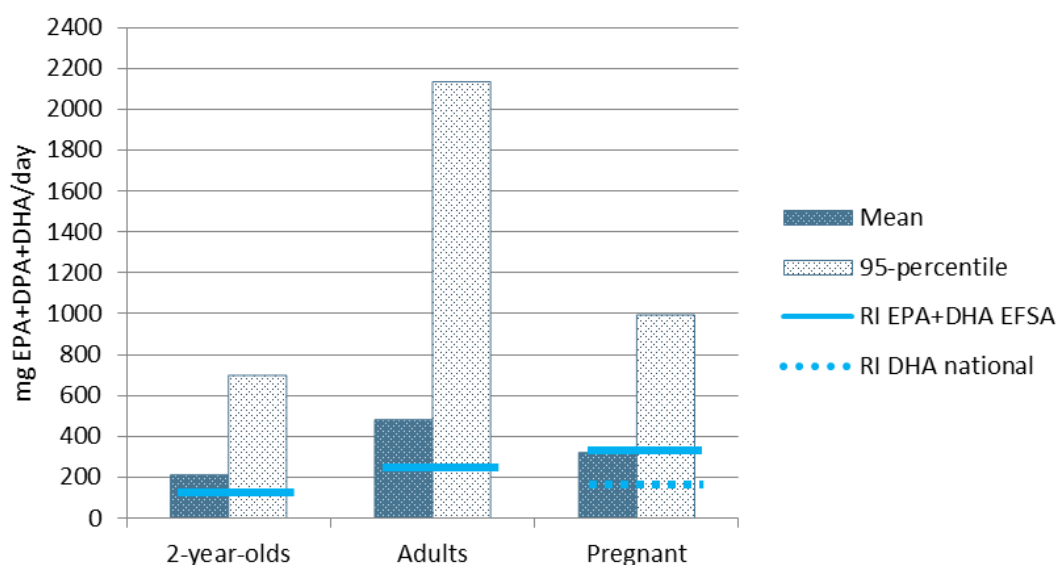


Figure 8.4.2.1-1 EPA+DPA+DHA contributed by fish in 2-year-olds, adults and pregnant women in relation to the recommended intake (RI). Blue solid lines indicate RI of 125 mg EPA+DHA per day in 2-year-olds, 250 mg EPA+DHA per day in adults (EFSA, 2010b), with an addition of 100 mg DHA per day (=350 mg) in pregnant women. DPA is not part of the RI and constitutes approximately 10% of the sum EPA+DPA+DHA. Blue dotted line indicates national RI of 200 mg DHA for pregnant women (Norwegian Directorate of Health, 2014). Since DHA constitutes about 80% of EPA+DPA+DPA, this is adjusted for in the figure. The 95th percentile for adults is considered an overestimate (Chapters 3 and 7).

8.4.2.2 Vitamin D

The Norwegian dietary recommendations (Norwegian Directorate of Health, 2014) of vitamin D are 10 µg/day for children and adults up to 75 years (Chapter 2.3). For adults above 75 years the recommendation is 20 µg/day.

Two-year-olds: The estimated daily intakes of vitamin D from mean and high (95th-percentile) fish consumption (0.51 and 1.3 µg) contribute with 5 and 13%, respectively, of the recommended daily intake.

Adults: The estimated daily intake of vitamin D contributed by average fish consumption (2.1 µg) corresponds to 21% of the recommended intake. Comparison of intake estimates of vitamin D and reference value is visualised in Figure 8.4.2.2-1. The 95th percentile for adults will reach the recommended intake, but is considered an overestimate (Chapters 3 and 7).

Pregnant women: The estimated daily intakes of vitamin D from mean and high (95th-percentile) fish consumption (0.96 and 2.3 µg) contributed with 10 and 23%, respectively, of the recommended daily intake.

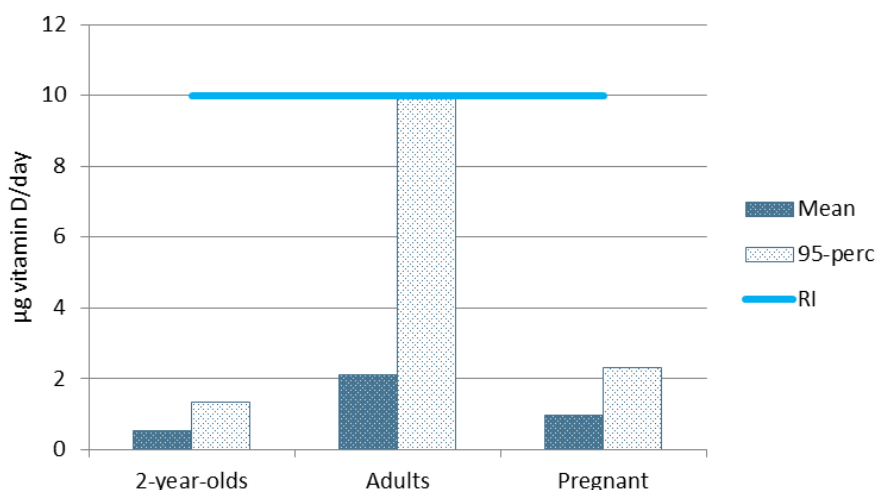


Figure 8.4.2.2-1 Vitamin D contributed by fish in 2-year-olds, adults (up to 70 years old) and pregnant women in relation to the recommended intake of 10 µg/day (RI, blue line). The 95th percentile for adults is considered an overestimate (Chapters 3 and 7).

VKM notes that fish consumption, mean or high, contributes from 5 to 23% of the recommended intake of vitamin D. However, in all three population groups, consumption of cod liver oil is common (37-68%), and daily consumption in amounts as suggested on the products will contribute with the recommended intake of vitamin D in children and adults under 75 years (10 µg), and with 50% of the recommended intake (20 µg) in adults above 75 (Chapter 7).

8.4.2.3 Iodine

The Norwegian dietary recommendations (Norwegian Directorate of Health, 2014) of iodine is 90 µg/day in 2-year-olds, 150 µg/day in adults, and 175 µg/day in pregnant women (Chapter 2.3).

Two-year olds: The estimated daily intakes of iodine from mean and high (95th percentile) fish consumption (35 and 82 µg) contribute with 39 and 91%, respectively, of the recommended daily intake (90 µg).

Adults: Fish consumption contributes on average with 86 µg iodine per day corresponding to on average 57% of the recommended intake (150 µg/day). The 95th percentile for adults is considered an overestimate (Chapters 3 and 7).

Pregnant women: The estimated daily intakes of iodine from mean and high (95th percentile) fish consumption (54 and 127 µg) contribute with 31 and 73%, respectively, of the recommended daily intake (175 µg).

Comparison of intake estimates of iodine and reference value is visualised in Figure 8.4.2-3 - 1.

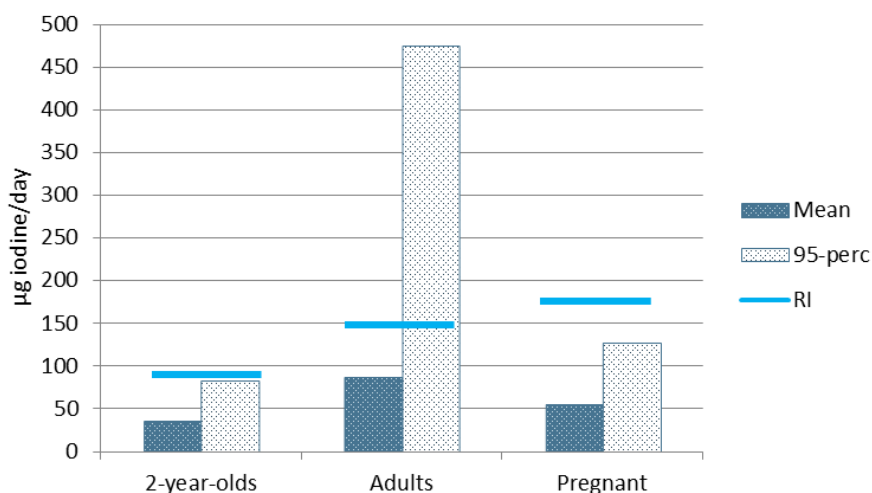


Figure 8.4.2.3-1 Iodine contributed by fish in 2-year-olds, adults and pregnant women in relation to the recommended intake (RI, blue lines, 90 µg/day in 2-year-olds, 150 µg/day in adults, 175 µg/day in pregnant women). The 95th percentile for adults is considered an overestimate (Chapters 3 and 7).

8.4.2.4 Selenium

The Norwegian dietary recommendations (Norwegian Directorate of Health, 2014) of selenium are 25 µg/day in 2-year-olds, in average 55 µg/day in adults (50 µg/day in women, 60 µg/day in men), and 60 µg/day in pregnant women (Chapter 2.3).

Two-year-olds: The estimated daily intakes of selenium from mean and high (95th percentile) fish consumption (4.5 and 12 µg) contribute with 18 and 48%, respectively, of the recommended daily intake (25 µg).

Adults: Fish consumption contributes on average with 15 µg selenium per day corresponding to 27% of the recommended selenium intake (30% in women and 25% in men). The 95th percentile for adults will reach the recommended intake, but is considered an overestimate (Chapters 3 and 7).

Pregnant women: The estimated daily intakes from mean and high (95th percentile) fish consumption (9.0 and 23 µg) contribute with 15% and 38%, respectively, of the recommended daily intake in pregnancy (60 µg).

Comparison of intake estimates of selenium and reference value is visualised in Figure 8.4.2-4-1.

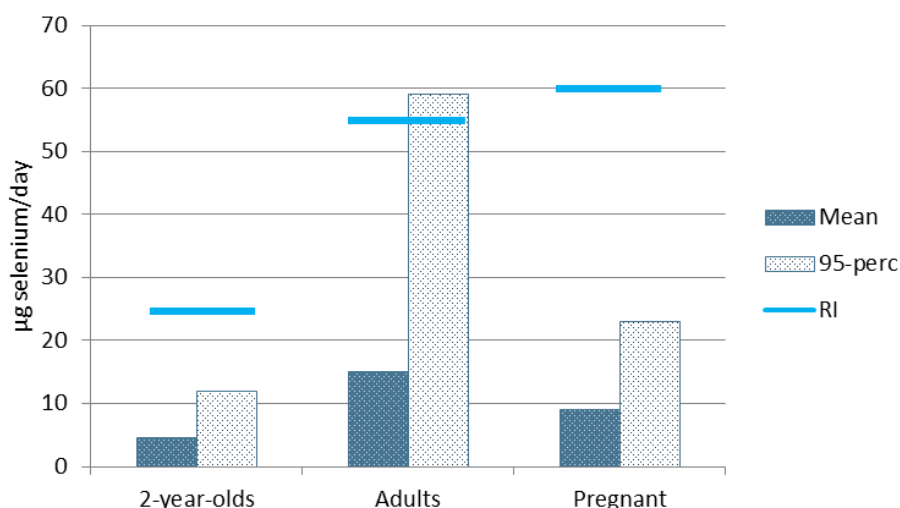


Figure 8.4.2.4-1 Selenium contributed by fish in 2-year-olds, adults and pregnant women in relation to the recommended intakes (RI, blue lines, 25 µg/day in 2-year-olds, 55 µg/day in adults (50 in women, 60 in men), 60 µg/day in pregnant women). The 95th percentile for adults is considered an overestimate (Chapters 3 and 7).

VKM concludes that with current average consumption of fish, the contribution of EPA and DHA from fish will reach the European recommended intake (EFSA, 2010b) of EPA and DHA for adults and 2-year-olds, while for pregnant women the intake is lower than recommended for this group. However, for pregnant women, the intake of DHA is sufficient to meet the national intake recommendation for pregnant women. For the high fish consumers, all age groups will reach the recommended intakes of EPA and DHA.

The contribution of dietary n-6 fatty acids from farmed salmon compared to the overall dietary intake of n-6 fatty acids is low (less than 3%).

For vitamin D, current fish consumption contributes approximately to 1/5 of the national recommended intakes for adults but less for pregnant women and 2-year-olds.

Furthermore, with current fish consumption, low intakes of selenium and iodine from fish relative to the national recommended values may be complemented by intake from a diversity of other dietary sources.

8.4.3 Comparison of nutrient intake estimates from scenarios with recommended intakes

VKM has made various scenarios to foresee how possible changes in fish consumption pattern and amounts will affect the contribution from fish to recommended intakes of specific essential nutrients. Since fatty fish is the most important dietary source for EPA and DHA (although lean fish also contributes depending on the amounts consumed), as well as of

vitamin D, scenarios of dietary intake of EPA and DHA as well as vitamin D, with current concentrations of these nutrients in farmed Atlantic salmon have been made. The present total mean fish consumption in the different age groups are used to model different consumption patterns, like increased intake of fatty fish to 50% of the total fish consumption, along with scenarios of all fish eaten being either lean (cod) or fatty fish (farmed Atlantic salmon).

Thus, the scenarios in Tables 8.4.3-1 and 8.4.3-2 are based on current concentrations of nutrients in cod and farmed Atlantic salmon, present consumption of fish, about 60 percent lean fish and 40 percent fatty fish, and possible changes in distribution of consumption of fatty and lean fish. Cod is used for lean fish, and farmed Atlantic salmon for fatty fish. In order to compare the intake of nutrients with the food-based dietary guidelines (Norwegian National Council for Nutrition, 2011), scenarios with 450 g fish consumption per week are also included.

8.4.3.1 Eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA) - scenarios

As demonstrated in Table 8.4.3.1-1, adults reach adequate intake of EPA+DHA (EFSA, 2010b) (Chapter 2.3) based on today's consumption of fish, and also for the scenarios including farmed salmon. The scenario where all fish consumed (450 g) is cod (lean fish) will give a mean intake of EPA+DHA below the recommended intake.

In 2-year-olds and pregnant women both today's intake and the scenarios based on cod give intakes of EPA+DHA below the recommended intakes.

Furthermore, a scenario mimicking today's food-based dietary guidelines for fish consumption (450 g fish of which 200 g is fatty fish), demonstrates that all age groups reach the recommended intakes of EPA and DHA if the fatty fish species is farmed Atlantic salmon with today's concentrations of EPA and DHA.

Fatty fish is, of course, the most important source of fatty acids, but also lean fish contributes to the intake depending on the amount consumed.

Table 8.4.3.1-1 Intake of sum EPA+DPA+DHA and different scenarios of fish intake in adults, 2-year-olds and pregnant women

Population groups	Recommended intake EPA+DPA+DHA mg/day	Today's mean intake of EPA+DHA mg/day	Intake by different scenarios of today's mean fish consumption			Intake by consumption of 450 g (225g) ^f fish/week		
			50% farmed salmon + 50% cod	mg/day Only cod ^d	mg/day Only farmed salmon ^e	40% farmed salmon +60% cod	mg/day Only cod ^d	mg/day Only farmed salmon ^e
2-y-olds	~125 ^a	204	127	44	210	221	88	421
Adult	~250 ^b	475	412	142	682	442	176	843
Pregnant women	~250 (+100-200 DHA) ^b 200 DHA ^c	312	246	85	406	442	176	843

^aAccording to EFSA, 2010b and adjusted for portion size for children being 50% of an adult portion of 150 g, ^b according to EFSA, 2010b, ^c according to Norwegian dietary recommendations (Norwegian Directorate of Health, 2014), which were based on the Nordic Nutrition Recommendations 5th edition (NNR5, 2012), ^dcod represents lean fish; ^efarmed Atlantic salmon represents fatty fish, ^ffor adults, the recommended fish consumption of 450 g/week is used, and half of this for 2-year-olds, i.e. 225 g fish per week.

8.4.3.2 Vitamin D - scenarios

It can be seen in Table 8.4.3.2-1 that for all population groups, fish consumption per se is not enough to reach the recommended intake of vitamin D (Norwegian Directorate of Health, 2014), see Chapter 2.3) neither with regard to today's intake (5-20% of recommended intake) nor with regard to the different scenarios.

Fatty fish species, like farmed Atlantic salmon, are more important sources of vitamin D than lean fish species.

The highest scenario based on an intake of 450 g farmed Atlantic salmon (225 g for 2-year-olds) per week will contribute to half the recommended vitamin D intake. By substituting all farmed salmon with the fatty fish species representing the highest (herring) and lowest (mackerel) fillet vitamin D concentration, the vitamin D intake from fish would nearly double and decrease to one third, respectively.

Table 8.4.3.2-1 Intake of vitamin D and different scenarios of fish intake in 2-year-olds, adults, and pregnant women

Population groups	Recommended intake of vitamin D µg/day ^a	Today's mean intake of vitamin D µg/day	Intake by different scenarios of today's mean fish consumption			Intake by consumption of 450 g (225g) ^d fish/week		
			50% farmed salmon + 50% cod	µg/day Only cod ^b	Only farmed salmon ^c	40% farmed salmon + 60% cod	µg/day Only cod ^b	Only farmed salmon ^c
2-y-olds	10	0.51	0.7	0.2	1.2	1.2	0.5	2.4
Adult	10	2.1	2.3	0.7	3.9	2.5	0.9	4.8
Pregnant women	10	0.96	1.4	0.4	2.3	2.5	0.9	4.8

^aaccording to Norwegian dietary recommendations (Norwegian Directorate of Health, 2014); ^bcod represents lean fish.

^cfarmed salmon represents fatty fish; ^dfor adults, the recommended fish consumption of 450 g/week was used, and half of this for 2-year-olds, i.e. 225 g fish per week.

8.4.3.3 Iodine – scenarios

It can be seen in Table 8.4.3.3-1 that for all population groups, fish consumption per se is not enough to reach the recommended intake of iodine (Norwegian Directorate of Health, 2014), see Chapter 2.3. Lean marine fish species, like Atlantic cod, are more important sources of iodine than fatty fish species. If today's consumption consists of only cod, adults will meet the recommended intake.

The highest scenario based on an intake of 450 g (225 g for 2-year-olds) Atlantic cod per week will meet the national recommended intake of iodine in all age groups.

Table 8.4.3.3-1 Intake of iodine and different scenarios of fish intake in 2-year-olds, adults and pregnant women

Population groups	Recommended intake of iodine $\mu\text{g/day}^a$	Today's mean intake of iodine $\mu\text{g/day}$	Intake by different scenarios of today's mean fish consumption			Intake by consumption of 450 g (225g) ^d fish/week		
			50% farmed salmon + 50% cod	Only cod ^b	Only farmed salmon ^c	40% farmed salmon + 60% cod	Only cod ^b	Only farmed salmon ^c
2-y-olds	90	35	26	52	0.64	63	104	1.3
Adult	150	86	85	168	2.1	126	208	2.6
Pregnant	175	54	51	100	1.2	126	208	2.6

^aaccording to Norwegian dietary recommendations (Norwegian Directorate of Health, 2014); ^bcod represents lean fish, ^cfarmed salmon represents fatty fish, ^dfor adults, the recommended fish consumption of 450 g/week was used, and half of this for 2-year-olds, i.e. 225 g fish per week.

VKM concludes that for 2-years-old and adult EFSA's recommended intake of EPA and DHA are met by the average fish consumption, while for pregnant women the intake is lower. For vitamin D, selenium and iodine current average or high fish consumption alone does not contribute sufficient amounts to meet the national recommendations. According to scenarios, increasing the consumption of fatty fish will increase the intake of vitamin D, EPA and DHA while increasing consumption of lean fish will increase the intake of iodine. Furthermore, VKM notes that the choice of fatty fish species, i.e. farmed Atlantic salmon, mackerel and herring is also of importance due to differences in nutrient concentrations.

8.5 Risk characterisation of undesirable substances in fish

High consumption of certain fish species may be associated with a relatively high exposure to contaminants and other undesired compounds that may be potentially hazardous to human health. The potentially highest risk from contaminants and other undesired compounds is posed by dioxins and dl-PCBs as well as methylmercury. These chemicals may cause various adverse health effects, and the most sensitive life stage for exposure is during foetal development (Chapter 3). Due to the physico-chemical properties of dioxins and PCBs, the highest levels are found in fatty fish, while the highest methylmercury levels are found in predatory fish high in the food chain, independently of percentage of fat in the fish. Lean species are the major sources in Norway. Methylmercury constitutes 80-100% of total mercury in fish. The contaminant levels and composition vary between fish species and within a species depending on factors like sex, age, size, trophic level, reproductive and nutritional status and environmental status.

8.5.1 Comparison of contaminants in fish; 2014 versus 2006

Both for wild caught fish, farmed fish and fish products, the data base on concentrations of specific contaminants, particularly mercury, dioxins and dl-PCBs has improved greatly since 2006 (Chapter 6). Thus, the uncertainties in the exposure estimates have been reduced.

Since 2006, more information is also available on occurrence and concentrations of other undesirable substances in farmed fish, such as pesticides and mycotoxins originating from new feed sources. Medicine residues from treatment of diseases in fish farming have been monitored according to production volume regulated by EU-directive 96/23.

Wild caught fish: For dioxins and dl-PCBs, consumption of fatty fish like mackerel, herring, wild salmon and trout contributes substantially to exposure. The available data for wild caught fish are not suitable to show time-trends of contaminant levels, e.g. regular sampling of the same species from the same area over a long period of time, however there seem to be minor or no changes of the composition and concentrations of contaminants in wild caught fish. There is, however, a decreasing trend of dioxins and dl-PCBs in the environment and therefore also in food like wild caught fish resulting in a decreased exposure for humans.

Lean fish like cod, even though the mercury level is low, is a substantial source of this contaminant in the Norwegian diet because of a relatively high consumption. High quality relevant time-trend data on mercury levels in fish are not available. Thus, temporal trends in fish cannot be elucidated. However, the exposure data indicates a modest higher exposure in children in the present assessment than in 2006. The methodological differences in food consumption surveys used in 2006 and 2014 prevent conclusions on differences in mercury exposure levels in adults (Chapters 3 and 7).

Farmed Atlantic salmon: Farmed Atlantic salmon is a dietary source of dioxins and dl-PCBs. Although there has been a decline in concentrations of dioxins and PCBs in some wild caught fish since 2006 (VKM; 2006), the corresponding decline in Atlantic salmon and in trout has been more pronounced since the raw materials used in feed for Norwegian farmed Atlantic salmon and trout have substantially changed since then (Chapter 5). Up to 70% of the fish meal and fish oil is replaced by plant proteins and vegetable oils, respectively, which has resulted in changes in composition and levels of contaminants in Atlantic salmon fillet since 2006 (VKM; 2006). The most important changes are shown in Table 8.5.1-1.

Table 8.5.1-1 Contaminant levels in farmed Atlantic salmon in 2006 and 2014

Year	Mercury mg/kg fillet	Sum dioxins and dl-PCBs ng TEQ/kg fillet
2006	0.030	1.7
2014	0.014	0.52
Change 2006 to 2014	~50% reduction	~70% reduction

VKM concludes that the most significant changes with regard to undesirable substances in fish are found for farmed Atlantic salmon where current concentrations of dioxins and dl-PCBs, and mercury, are reduced to about 30 and 50%, respectively, of the corresponding levels in 2006. There are minor or no changes in concentrations of dioxins and dl-PCBs and mercury in wild fish species since 2006, however, the suitability of the databases is not optimal to reveal time-trends.

8.5.2 Comparison of contaminant exposure estimates with tolerable intakes

In the following, dietary exposure to contaminants contributed by fish is compared with the tolerable intakes (Chapter 7). A tolerable intake is the amount of a substance, or substance group, which can be consumed safely throughout a person's lifetime without appreciable risk of adverse health effects. Tolerable intakes are set by large international risk assessment bodies, such as WHO or EFSA, and incorporate safety margins, in order to protect all parts of the population (Chapter 2.3).

Regarding the environmental contaminants brominated flame retardants, VKM refers to the conclusions in a risk assessment from EFSA in 2011 that the health risk associated with the current exposure to these compounds is low. The amount of fluorinated compounds such as PFOS and PFOA in the Norwegian diet is much lower than what is tolerable according to an EFSA assessment in 2008 (Chapter 2).

8.5.2.1 Mercury

The tolerable weekly intake (TWI) for methylmercury is 1.3 µg/kg bw (EFSA, 2012a) (Chapter 2.3).

Two-year olds: Both mean and high mercury exposure (95th percentile) is below the tolerable weekly intake.

Pregnant women: The exposure is lower than the tolerable intake. This includes high fish consumers, which were represented in the high percentiles (95th and 97.5th percentiles) of mercury exposure.

Adults: Mean mercury exposure is below the tolerable weekly intake, as well as the 95th percentile although it represents an overestimation (Chapter 3 and introduction to Chapter 7).

Comparison of exposure estimates and tolerable weekly intake (TWI) is visualised in Figure 8.5.2.1-1.

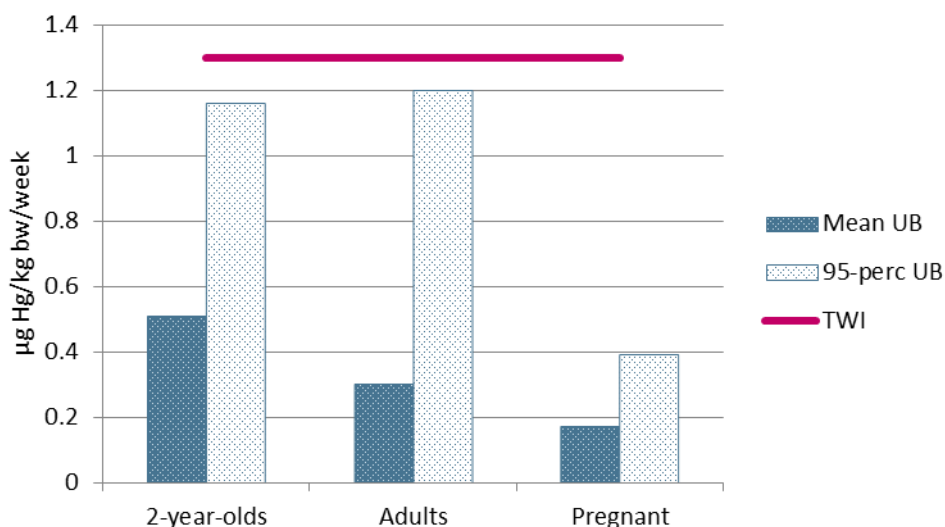


Figure 8.5.2.1-1 Mean upper bound (UB) exposure to mercury (Hg) from fish in 2-year-olds, adults, and pregnant women in relation to the tolerable weekly intake of 1.3 µg/kg bw/week (TWI, red line). The 95th percentiles are also shown, which for adults is an overestimate (Chapters 3 and 7).

There are no other substantial dietary sources to methylmercury than fish in the Norwegian diet. The exposure estimate is based on mean occurrence of mercury in fish, and exposure may be higher if fish with higher concentrations is consumed regularly, i.e. fish from contaminated coastal areas. The Norwegian Food Safety Authority issues restrictions for consumption of fish from contaminated areas.

8.5.2.2 Dioxins and dioxinlike PCBs

Tolerable weekly intake for dioxins and dl-PCBs is of 14 pg TEQ/kg bw (SCF, 2001) (Chapter 2.3).

Two-year-olds: Neither mean nor high exposures (95th percentile) to dioxins and dl-PCBs from fish alone exceed the TWI. High exposure makes up 52% (LB) to 67% (UB) of the TWI (Figure 8.5.2.2-1). The higher exposure in 2-year-olds than in adults can be explained by higher food consumption per kg bw in children than in adults.

Adults: Exposure from fish does not exceed the TWI (Figure 8.5.2.2-1). In high fish consumers (95th percentile exposure) the weekly exposure constitutes 41% (LB) to 50% (UB) of TWI.

Pregnant women: The UB mean and 95th percentile weekly intakes from fish are 0.94 and 2.7 pg TEQ/kg bw respectively, and the 95th percentile UB exposure constitutes 19% of the tolerable weekly intake. The 97.5th percentile exposure is 3.7 pg TEQ/kg bw/week and contributes with 26% of the TWI.

The contribution to total exposure from other food commodities has not been included in any of the age groups, and the exposure from fish oil also comes in addition.

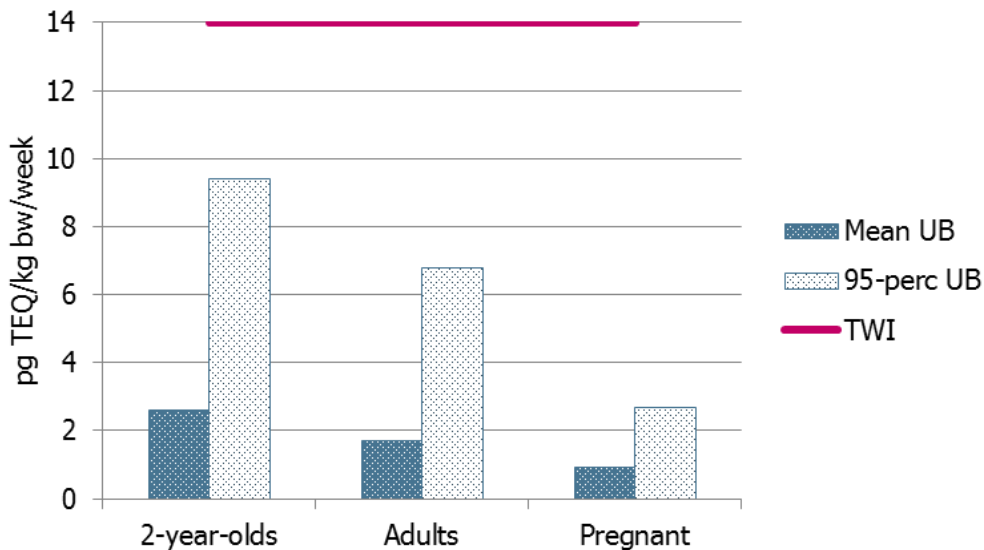


Figure 8.5.2.2-1 Mean upper bound (UB) exposure to dioxins and dl-PCBs **from fish** in 2-year-olds, adults, and pregnant women in relation to the tolerable weekly intake of 14 pg TEQ/kg bw (TWI, blue line). The 95th percentile for adults is an overestimate (Chapters 3 and 7).

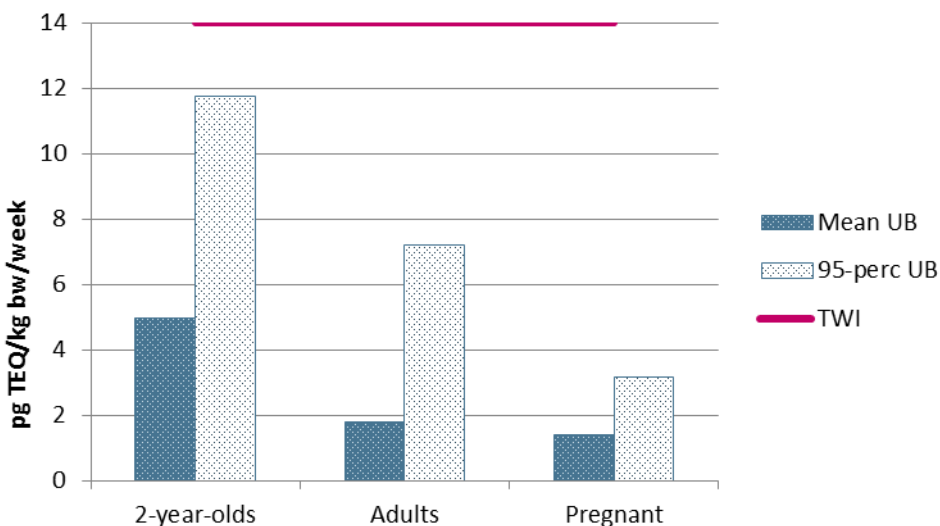


Figure 8.5.2.2-2 Mean upper bound (UB) exposure to dioxins and dl-PCBs **from fish as food and 5ml cod liver oil** in 2-year-olds (Småbarnskost 2007), adults (Norkost 3) and pregnant women (MoBa) in relation to the tolerable weekly intake of 14 pg TEQ/kg bw (TWI, red line). Mean exposure from 5 ml cod liver oil has been added to the exposure from fish both at the mean and the 95th percentile exposure from fish. The 95th percentile for adults is an overestimate (Chapters 3 and 7).

The recommended daily intake of cod liver oil represents a mean exposure of 0.11 (LB) to 2.34 (UB) pg/TEQ/kg bw/week, dependent on the body weight and comes in addition to exposure from fish among consumers (illustrated in Figure 8.5.2.2-2). The relatively high contribution from fish oils in 2-years olds compared to adults can be explained by the low body weight in children, whereas the recommended daily volume of fish oil is similar as in adults.

VKM concludes that with the present mean level of mercury in fish and the present fish consumption in Norway, the methylmercury exposure from fish being below the TWI of 1.3 µg/kg bw/week for more than 95% of the population of 2-year-olds, adults and pregnant women, represents negligible risk and is of no concern.

With the present mean level of dioxins and dl-PCBs in fish and the present fish consumption in Norway, high fish consumption (the 95th percentile) contributes with up to 50, 19, 67% of the TWI of 14 pg TEQ/kg bw/week for adults, pregnant women and 2-year-olds respectively. Daily consumption of cod liver oil or fish oil (which is common in all population groups) in amounts as suggested on the product will in addition contribute with 0.8 to 16% of the TWI, depending on the body weight. With the present TWI and taking into consideration that fish and fish products are main contributors to dioxins and dl-PCBs in the Norwegian diet, VKM concludes that the exposure from fish to dioxins and dl-PCBs represents negligible risk and is of no concern.

8.5.3 Comparison of other undesirable substances in farmed fish fillet with maximum residue limits and levels (MRLs)

To avoid the presence of residues of veterinary medicinal products (VMPs) at levels that might cause harm for the consumers, acceptable legal residue concentrations (MRL) in food producing animals have been established. A maximum residue limit (MRL) is the highest permitted residual concentration of legally applied pharmacologically active substances in products (food) intended for human consumption. Consumption of food with medicine residues below the MRL should, by a wide safety margin, not pose any health risk to the consumer. When setting MRLs, eventual effects of VMPs on future processing of food, and if the VMP has additional use (e.g. as pesticide) which could lead to additional exposure for the consumer, are taken into account. The MRLs for fish are set for muscle and skin in natural proportions. For more details, see Chapter 2.2.4.

No residues of banned substances or residues above EU maximal residue limits for veterinary medicinal products have been detected in any of the about 30 000 samples from farmed fish (1998-2013). The residues controlled include e.g. antibiotics and agents against sea lice.

VKM is of the opinion that the present exposure to veterinary medicine residues including residues of antibiotics in farmed fish in the Norwegian diet is of no concern since the levels are very low and often not detectable even with sensitive analytical methods.

For new contaminants in fish feed like the pesticide endosulfan, polycyclic aromatic hydrocarbons (PAH) and mycotoxins, VKM is of the opinion that their concentration in farmed fish in the Norwegian diet is likely not a food safety issue

since the concentrations are very low and often not detectable even with sensitive analytical methods.

With regard to the synthetic antioxidants (ethoxyquin (EQ), butylhydroksyanisol (BHA) and butylhydroksytoluen (BHT)), as well as the pesticide endosulfan, the calculated exposures from a 300 g portion of farmed fish fillets are reported to be below their respective ADIs and therefore of no concern.

8.5.4 Scenarios on dietary exposure of contaminants in farmed salmon with changed composition of lean and fatty fish

VKM has made various scenarios to foresee how possible changes in fish consumption pattern and amounts will affect the exposure from fish to tolerable intakes (TWI) of mercury, dioxins and dl-PCBs.

Since lean fish is the only substantial dietary source of mercury, and fatty fish is an important dietary source for dioxins and dl-PCBs (although there are other food sources than fish for these contaminants), scenarios of dietary exposure to mercury, and dioxins and dl-PCBs, with today's concentrations of these contaminants in farmed Atlantic salmon have been made. The total mean fish consumption in the different age groups are used to model different consumption patterns, like increased intake of fatty fish to 50% of the total fish consumption, along with scenarios of all fish eaten being either lean (cod) or fatty fish (farmed Atlantic salmon).

Thus, the scenarios in Tables 8.5.4.1-1 and 8.5.4.2-1 og 2 are based on current concentrations of mercury, and dioxins and dl-PCBs in farmed Atlantic salmon, today's consumption of fish, and possible changes in distribution of consumption of fatty and lean fish. Cod is representing lean fish, and farmed Atlantic salmon fatty fish. In order to compare the intake of contaminants with the food based dietary guidelines (Norwegian Directorate of Health, 2014), scenarios with 450 g fish consumption per week are also included.

8.5.4.1 Mercury - scenario

As demonstrated in Table 8.5.4.1-1 and based on current consumption of fish, about two third lean fish and one third fatty fish, the exposure to mercury is below the TWI of 1.3 µg/kg bw/week (20-40% of the TWI) in all population groups. If only farmed salmon is consumed, the mercury exposure is less than 10% of the TWI. If all fish consumed by adults is lean fish (cod), approximately 450 g cod per week, fish consumption will contribute to about 40% of the mercury TWI. For 2-year-olds, 225 g lean fish (cod) per week will contribute with mercury exposure similar to the TWI. By substituting cod with farmed Atlantic salmon, the mercury exposure from lean fish will decrease with around 70%.

Estimates in Table 8.5.4.1-1 are based on the mean body weights reported in Småbarnskost 2007, Norkost 3 and MoBa.

Table 8.5.4.1-1 Exposure to methylmercury ($\mu\text{g MeHg}$ as Hg/kg bw/week) and different scenarios of fish intake in adults, 2-year-olds and pregnant women

Population groups	Tolerable weekly intake (TWI) ^a $\mu\text{g Hg/kg bw/week}$	Exposure by today's mean fish intake ^b $\mu\text{g Hg/kg bw/week}$	Exposure by different scenarios of today's mean fish intake per week $\mu\text{g Hg/kg bw/week}$			Exposure by intake of 450 g (225g) ^e fish/week $\mu\text{g Hg/kg bw/week}$		
			50% farmed salmon + 50% cod	Only cod ^c	Only farmed salmon ^d	40% farmed salmon + 60% cod	Only cod ^c	Only farmed salmon ^d
2-year-olds	1.3	0.51	0.40	0.70	0.10	0.90	1.3	0.30
Adults	1.3	0.30	0.21	0.35	0.07	0.29	0.44	0.08
Pregnant women	1.3	0.17	0.14	0.24	0.05	0.34	0.50	0.09

^aaccording to (EFSA, 2012a)

^bupper bound means of total exposure of Hg from fish are used, see Table 7.1.2.2-1, Table 7.1.2.3-1, Table 7.1.2.4-1.

^ccod represents lean fish.

^dfarmed Atlantic salmon represents fatty fish.

^efor adults, the recommended fish consumption of 450 g/week was used, and half of this for 2-year-olds, i.e. 225 g fish per week

8.5.4.2 Dioxins and dioxin-like PCBs - scenario

Based on today's consumption of fish, about two thirds lean fish and one third fatty fish, the exposure to dioxins and dl-PCBs is below the tolerable weekly intake (TWI) of 14 pgTEQ/kg bw (13-19% of TWI) for all population groups (Table 8.5.4.2-1).

Fatty fish species like mackerel, herring and salmon have relatively high concentrations of dioxins and dl-PCBs, and therefore contribute to exposure to these contaminants. In Table 8.5.2.2-1, it is shown that if only farmed Atlantic salmon is consumed, the fish contributes with 11-31% of the TWI of dioxins and dl-PCBs for all population groups.

If adult consumption is set to 450 g farmed salmon per week, the fish consumption will contribute to about 21% (adults and pregnant women) of the TWI. For 2-year-olds, 225g farmed salmon per week will contribute with about 63% of the TWI.

By substituting all farmed salmon with mackerel the dioxins and dl-PCBs exposure will increase with around 60% compared with farmed Atlantic salmon.

Table 8.5.4.2-1 Exposure to dioxins and dl-PCBs (pg TEQ/kg bw/week) from different scenarios of fish intake in adults, 2-year-olds and pregnant women

Population groups	Tolerable weekly intake (TWI) ^a pg TEQ/kg bw/week	Exposure by today's mean fish intake ^b pg TEQ/kg bw/week	Exposure by different scenarios of today's mean fish intake/week pg TEQ/kg bw/week			Exposure by consumption of 450 g (225g) ^e fish/week pg TEQ/kg bw/week		
			50% farmed salmon +50% cod	Only cod ^c	Only farmed salmon ^d	60% lean fish +40% fatty fish	Only lean fish ^c	Only fatty fish ^d
2-year-olds	14	2.6	2.5	0.49	4.4	4.1	0.98	8.8
Adults	14	1.7	1.3	0.26	2.3	1.4	0.33	2.9
Pregnant women	14	0.94	0.90	0.18	1.6	1.6	0.38	3.4

^aaccording to SCF (2001).

^bupper bound mean of total exposure of sum dioxins and dl-PCBs from fish is used, see Table 7.1.2.2-2.

^ccod represents lean fish.

^dfarmed Atlantic salmon represents fatty fish.

^efor adults, the recommended fish consumption of 450 g/week was used, and half of this for 2-year-olds, i.e. 225 g fish per week.

VKM is of the opinion that there is negligible risk associated with eating lean or fatty fish with the present concentrations of dioxins and dl-PCBs, and mercury, in amounts equivalent to the present mean weekly fish consumption for 2-year-olds, pregnant women and adults since exposures are below the respective TWIs.

Based on these scenarios, VKM is of the opinion that fish consumption in line with the food-based dietary guideline of 300-450 g fish, hereof 200 g fatty fish per week, does not contribute with exposures to dioxins and dl-PCBs and mercury from either lean or fatty fish exceeding the respective TWIs. Fish consumption in line with the food based dietary guideline of 450 g fish per week is therefore of no concern from a contaminant exposure perspective.

8.5.5 Scenarios on changing dietary exposure to dioxins and dl-PCBs from farmed Atlantic salmon

In the above described scenarios, VKM has considered only exposure to dioxins and dl-PCBs from fish. Since there are other food sources in the Norwegian diet that contribute to the exposure to these contaminants, a simple model estimate of weekly intake of dioxins and dl-PCBs in adults from various amounts of farmed salmon and other food has been done.

Even though the change in feed composition since 2006 has reduced the concentrations of dioxins and PCBs in farmed Atlantic salmon fillets (by about 70%), the levels can be further reduced by decontamination of the fish oil included in the feed without reducing the composition and levels of EPA and DHA (see Chapter 6 for details). Thus, VKM also made

scenarios where concentrations of dioxins and PCBs have been lowered by decontamination of the fish oil.

Thus, in figure **8.5.5-1**, simple model estimates of weekly intake of dioxins and dl-PCBs in adults for consumption of various amounts farmed salmon with different levels of contamination are shown. The levels of contamination given represent both farmed Atlantic salmon grown on feed prepared with cleaned fish oil (0.2 pg TEQ per kg filet), the present mean upper bound concentration found in farmed Atlantic salmon (0.5 pg TEQ per g filet), and the maximum upper bound value of the present concentration in farmed Atlantic salmon (1.5 pg TEQ per g filet) (Table 6.2.1.2-1). The category "other food" is the estimated sum of weekly intake of contaminants from other food than fish (2.8 pg TEQ/kg bw/week, based on results in Caspersen et al. (2013), personal communication, IH Caspersen), and the recommended daily intake of cod liver oil (0.55 pg TEQ/kg bw/week). The horizontal unbroken red line represents the tolerable weekly intake (TWI) for dioxins and dioxin-like PCB (14 pg TEQ per kg bw). Generally, an adult fish serving is equivalent to about 150-200 g fish.

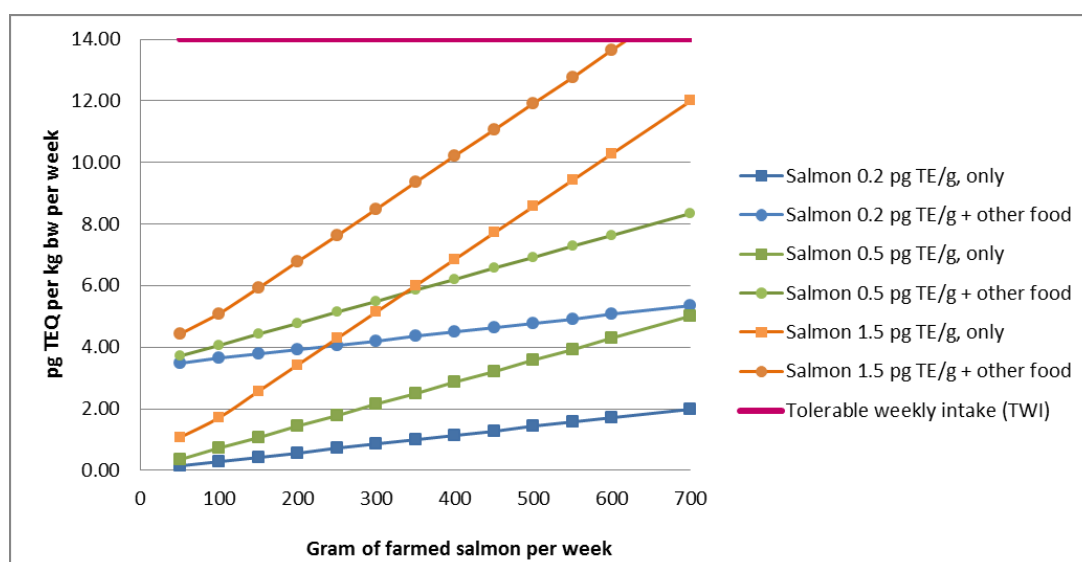


Figure 8.5.5-1 Illustration of weekly consumption of farmed fish and the concurrent exposure to dioxin and dioxin-like PCBs dependent on level of contamination and amount of consumption. "Other food" includes background exposure and exposure from cod liver intake.

Thus, consumption of other food and 600 g farmed salmon per week with the current concentrations of dioxins and dl-PCBs (0.5 pg/TEQ/g fish), contributes with about 60% of the TWI. Furthermore, when taking into consideration background exposure including cod liver oil, and based on Figure 8.5.5-1 it can be seen that TWI will not be exceeded even if an adult consumes either 600 g farmed Atlantic salmon with the current highest concentration of dioxins and dl-PCBs (1.5 pg/TEQ/g fish) or 1400 g farmed Atlantic salmon with the current mean concentration of dioxins and dl-PCBs (0.5 pg TEQ/g fish), which will represent 4 or 9 dinner servings per week, respectively.

In comparison, an adult can consume 800 g mackerel weekly (representing 5 dinner servings per week) with current mean concentration of dioxins and dl-PCBs (0.9 pg/TEQ/g fish) without exceeding TWI.

VKM is of the opinion that from a contaminant exposure perspective there is negligible risk for adults associated with eating farmed Atlantic salmon in amounts equivalent to 1400 g weekly (representing 9 weekly dinner servings) with the present mean concentration of dioxins and dl-PCBs since TWI is not exceeded even when exposure to dioxins and dl-PCBs from other food including cod liver oil is taken into consideration.

8.6 Benefit – risk comparison

Taking the present-day levels of nutrients and contaminants in fish, and the consumption of fish in different population groups in Norway into account, VKM concludes that:

The consumption of fish in Norway differs from the situation in many other countries in that the amount of fish is high and that the proportion of lean fish is large. Norwegians also eat fish in the form of cold cuts and spread since several meals per day may consist of open faced sandwiches. Adults eat on average 364 g/week (equivalent to 2-3 fish dinner servings per week given a portion size of 150 g), pregnant women eat 217 g/week (equivalent to 1-2 dinner serving per week given a portion size of 150 g), while 2-year-olds eat 112 g/week (equivalent to 1-2 dinner serving per week given a portion size of 75 g). Two thirds of the consumption consists of lean fish and minced fish products. Pregnant women eat fatty fish in amounts equivalent to less than half a dinner serving per week. VKM concludes that of the different population groups, only adults (18-70 years of age) reach the food based dietary guidelines for fish consumption (Norwegian Directorate of Health, 2014), while the fish consumption of children (2-year-olds) and pregnant women is lower.

From **a nutrient benefit assessment perspective**, VKM is of the opinion that for the different age groups, increase in both lean and fatty fish consumption will improve the role of fish as a source for important nutrients (EPA+DPA+DHA, vitamin D, iodine and selenium) relative to recommended intakes. Increased consumption of fatty fish will increase the intake of EPA+DPA+DHA and vitamin D, while an increase in the consumption of lean fish will increase the intake of iodine. Generally, an increase of marine fish consumption will increase the intake of selenium.

From **a benefit assessment perspective**, VKM is of the opinion that the average fish consumption in Norway for adults should give substantial benefit (positive health effects) with regard to specific cardiovascular disease. Pregnant women, who eat little or no fish, may miss the beneficial effects of fish consumption on neurodevelopmental outcomes in foetuses and infants.

From **a risk perspective** it is the opinion of VKM that with the present concentrations of dioxins and dl-PCBs, and mercury, the exposure to these compounds is below the tolerable intakes when fish is consumed in accordance with the dietary advice of 300-450 g fish (representing 2-3 dinner servings) hereof 200 g fatty fish per week and is therefore of no concern. This also applies if the fish consumed in adults consist of 1400 g farmed Atlantic salmon (representing 9 dinner servings) or 800 g mackerel weekly (representing 5 dinner servings). VKM is of the opinion that the present exposure to medicine residues including residues of antibiotics, new contaminants like the pesticide endosulfan, polycyclic aromatic hydrocarbons (PAH) and mycotoxins, and synthetic antioxidants (ethoxyquin (EQ), butylhydroksyanisol (BHA) and butylhydroksytoluen (BHT)) in farmed Atlantic salmon are of no concern.

Regarding the environmental contaminants brominated flame retardants, VKM refers to the conclusions in a risk assessment from EFSA in 2011 that the health risk associated with the current exposure to these compounds is low. The amount of fluorinated compounds such as PFOS and PFOA in the Norwegian diet is much lower than what is tolerable according to an EFSA assessment in 2008 (Chapter 2).

Following a comprehensive assessment of the scientific literature on the positive health effects of fish consumption and the contribution from fish to intake of beneficial compounds as well as exposure to hazardous contaminants in Norway, VKM concludes that the benefits clearly outweighs the negligible risk presented by current levels of contaminants and other known undesirable substances in fish. Furthermore, in Norway, adults including pregnant women with fish consumption less than one serving per week may miss the beneficial effects on cardiovascular diseases and optimal neurodevelopment in the fetuses and infants. In contrast to the conclusion in 2006, VKM concludes that there is no reason for specific dietary limitations on fatty fish consumption for pregnant women.

9 Uncertainties

This benefit-risk assessment is composed of several different parts. Various databases are used, including data on levels of nutrients and contaminants in fish feed and fish which may all contain uncertainties which in turn may influence the overall assessment. Furthermore, there may be uncertainties in the estimated fish consumption data retrieved from the dietary food surveys and there may be weaknesses in the epidemiological studies about health effects of fish consumption. The uncertainties associated with the different parts of this benefit-risk assessment are explained below.

9.1 Methodological challenges for assessing dietary consumption of fish, intake of nutrients and exposure to contaminants

9.1.1 Dietary assessment

Every dietary assessment is connected with uncertainty. A description of the most important uncertainties and assumptions in the dietary exposure calculations is described below.

Three concepts are fundamental to understanding the limitations of dietary assessment: habitual consumption, validity and precision (Livingstone and Black, 2003).

The habitual consumption of an individual is the person's consumption averaged over a prolonged period of time, such as weeks and months rather than days. However, this is a largely hypothetical concept; the consumption period covered in a dietary assessment is a compromise between desired goal and feasibility. In the dietary surveys used in this report the time periods covered are 14-days among the 2-year-olds (Småbarnskost 2007), the first 4-5 months of pregnancy in the MoBa-cohort (Brantsaeter et al., 2008; Meltzer et al., 2008), and two non-consecutive days at least one month apart among the adults (Norkost 3). The different time periods covered gives a challenge when comparing the fish consumption results from the three dietary assessment methods. The mean consumption can be considered comparable between the different dietary assessment methods; however, for the high percentiles the use of two 24-hour recalls has shown to be a problem. Twenty-four-hour recalls capture rich information on food consumption, but suffer from inadequately measuring usual intakes of weekly but not daily consumed foods like fish and fish products (Subar et al., 2006). Even when two 24-hour recalls are collected, the probability of consumption for most foods is poorly captured at the individual level.

However, the European Food Consumption Survey Method project has recommended to apply 24-hour recalls on at least two non-consecutive days per participant as the primary instrument for food consumption surveys (Brussaard et al., 2002), to account for intra-individual variation.

When only two days of food intake are the basis for the fish consumption in Norkost 3, persons that have eaten fish for dinner on both recall-days will be represented in the 95th percentile. It is unlikely that even a high fish consumer eats fish every day for a prolonged time, and therefore, the mean fish consumption over the two consumption days among those who reported fish for dinner both days represents an overestimate when it is transferred to weekly fish consumption. Also, many participants with no registered fish intake during the two 24-hour recalls will usually eat fish. This leads to a lower median weekly intake compared to a food-frequency method. Results from the Food propensity questionnaire are therefor included in this opinion (Chapter 3), as background for further discussion of the uncertainty of the fish intake.

Portion size estimation is one of the important sources of uncertainty in dietary assessment of the individual, especially for the 24-hour recall method where the participant is asked to accurately recall, describe, and quantify the food items and ingredients of mixed dishes that were consumed the previous day (Souverein et al., 2011). However, portion sizes of fish and fish products might not be among the most difficult foods to estimate, as fish cakes, fish fingers and tins of mackerel in tomato come in recognisable units and thus have less influence on the uncertainty.

The validity of a dietary assessment method refers to the degree to which the method actually measures the aspect of diet that it was designed to measure (Nelson and Margetts, 1997). Lack of validity is strongly associated with systematic errors (Burema et al., 1988). With systematic errors all respondents in a dietary study or each subgroup in a population produce the same type of error, like systematic underestimation or overestimation of intake. There is no dietary assessment method that measures the habitual diet without error, and thorough validation is required for all dietary assessment methods.

The FFQ used for the 2-year-olds were a slightly modified version of a FFQ that has been validated. The results from the validation showed fair agreement for most nutrients, but a significantly higher energy intake were reported with the FFQ than with the reference method, weighed record (Andersen et al., 2003; Andersen et al., 2004; Andersen et al., 2009).

The validation study of the MoBa FFQ showed fair agreement between food and nutrient intakes relative to the weighed record reference method. Furthermore, the estimated intakes of main food groups including seafood and supplementary n-3 fatty acids were reflected by biological markers (Brantsaeter et al., 2007b; Brantsaeter et al., 2009; Brantsaeter et al., 2007a; Brantsaeter et al., 2010).

The results of the validation of the Norwegian 24-hour recall method used among adults in Norkost 3 have not been published yet (A.M.W. Johansen et al., UiO, pers. comm.). When evaluating the energy intake with the Goldberg and Black cut off values (Black, 2000), the results showed that 16% of the participants in Norkost 3 underreported the energy intake, while 1.5% overreported the total energy intake (Totland et al., 2012). Other similar 24-hour recall methods have been validated and show an underestimation in energy intake of around

15% (Poslusna et al., 2009; Subar et al., 2003). Underestimation of energy intake indicates that not all foods eaten are reported, but not which foods are underreported.

It has been shown that foods perceived as unhealthy such as fats, sweets, desserts and snacks tend to be underreported to a larger degree than foods perceived as healthy (Olafsdottir et al., 2006). However, among children and adolescents there have been studies where this selective underreporting was not shown (Lillegaard and Andersen, 2005; Sjoberg et al., 2003). As the fish and fish products are perceived by most to be healthy foods, it might lead to a certain overestimation of reported intake. On the other hand, if underreporting of fish and fish products is of the same magnitude as for total energy, the estimates for fish used in the exposure calculations can also be underreported.

The precision of a technique is one that gives the same answer on repeated administrations (Livingstone and Black, 2003). Poor precision derives from large random errors in the techniques of dietary assessment. The effect of random errors can be reduced by increasing the number of observations, but cannot be entirely eliminated (Rothman, 2002).

The data collections of the different dietary surveys were performed from 2003 till 2011, and most of the contaminant data are from the same period 2006-2012. Dietary patterns are constantly changing. In a cohort study with a long data collection period, like in the MoBa study, changes in fish consumption during the study period has been documented (Caspersen et al., 2013).

MoBa is one of the largest pregnancy cohorts in the world and dietary data from 86 277 pregnancies was available for this report. However, the participation rate in MoBa is a concern. Of those invited during the years from 1999-2008, 40.6% consented to participate. Studies have shown that women in MoBa are older, better educated, and less often smokers compared with the general pregnant population. However, despite differences in the prevalence of exposures and outcomes between cohort participants and the general pregnant population, no statistically significant differences in associations between exposures and outcomes, e.g. prenatal smoking and low birth weight, maternal vitamin use and placental abruption, and parity and preeclampsia (Nilsen et al., 2013b; Nilsen et al., 2009). The cross sectional studies Norkost 3 and Småbarnskost 2007 also have rather low participation rates with 37% and 56%, respectively. It is unclear to which extent a low participation rate will influence the assessment of exposures contributed by fish. It has been shown that health-conscious people are more likely to participate in a dietary survey. This can indicate a somewhat different dietary pattern among the participants than among the whole population. The direction of the uncertainty is difficult to estimate. Health-conscious people tend to choose a more diverse diet, and even if the majority of the population (Norkost 3), 97%, reported to eat fish at least once a month, it might be that health-conscious people eat fish more often.

Individual consumption data reported in the dietary surveys have been paired with person specific self-reported body weights for the same individuals. However, when no body weights were given the mean body weights from the studies were imputed in 2-year-olds and adults.

9.1.2 Gender and body weight

Fish consumption was not divided by gender. The fish consumption among 2-year-olds was not significantly different between the genders (Kristiansen et al., 2009). For the contaminants, person specific body weights were used. This approach gave a good understanding of the diversity in the population. For the nutrients the intake was not divided by body weight, and therefore the level of intake will be somewhat higher in men than the average values given in this report, while the level of intake of nutrients for women will be somewhat lower.

9.1.3 Analytical measurements

The exposure estimates were based on levels in raw fish. There may be a certain reduction and/or increase of nutrients and contaminants during food processing. For instance, whereas loss of water during food preparation may lead to increased concentration of protein- or lipid-associated substances, loss of lipids or water-soluble substances into cooking water may be associated with decrease in concentration. However, such changes are considered to be relatively small (Jakobsen and Knuthsen, 2014; Rana and Raghuvanshi, 2013), compared with other uncertainties. The changes of nutrients and contaminants during food processing are not included in the exposure estimates in this report.

Any uncertainties related to the representativeness of the sampling of fish are described for each species, number and type of sample in Appendix VI.

There are always uncertainties related to analytical measurements. The methods used in fish surveillance, and which are used to analyse the contaminants and nutrients given in this report, are accredited and quality checked by Norwegian Accreditation. Still each single method has uncertainty, a limit of detection (LOD) and a limit of quantification (LOQ). The methods used are harmonized with methods from NMKL (Nordisk metodikk komité), and CEN (European Committee for Standardization). The principles for each method can be found in Appendix VI, together with references to each single method description.

The use of upper bound (UB) for dioxins and dl-PCBs most likely represents an overestimate of the exposure. For lower bound (LB), concentrations lower than the LOQ or LOD are substituted with zero. This most likely represents an underestimate of the exposure.

For commercial products containing fish like fish cakes and fish balls, nutrient and contaminant data for cod have been used. This might represent both underestimation and overestimation of both the intake and exposure estimations of nutrients and contaminants, respectively.

9.2 Epidemiological studies

There are uncertainties related to all kind of epidemiological studies, e.g. inclusion and exclusion criteria, serving size, type of fish consumed, type of subjects i.e. healthy, healthy but at high risk of cardiovascular disease or patients.

Criteria for objectively evaluating the level of causality of associations observed in epidemiology were stated by Hill (1965). These criteria, which include consistency and strength of the association, dose-response, time order, specificity, consistency on replication, predictive performance, biological plausibility and coherence, must be applied when discussing the results observed in every study.

In epidemiological studies, there is uncertainty related to the exposures as well as the health outcomes, and there is uncertainty related to whether reported effects are indeed related to the exposure and not confounded by other factors correlated with exposures and outcomes such as e.g. demographic factors, lifestyle, and home environment. Epidemiological studies use statistical models to adjust for confounding factors, but the possibility of unmeasured or residual confounding cannot be excluded. Misclassification of dietary exposure is likely to attenuate the effect-estimates in studies of diet and disease (Parr et al., 2006).

9.3 Summary of uncertainties

Evaluations of the overall effect of identified uncertainties are presented in Table 9.3-1, highlighting the main sources of uncertainty and indicating whether the respective source of uncertainty might have led to an overestimation or underestimation of the exposure and/or the resulting risk or benefit (EFSA 2006).

Table 9.3-1 Qualitative evaluation of influences of uncertainties on the benefit and risk assessment of intake of nutrients and exposure of contaminants from fish and fish products

Source of uncertainty	Direction
Dietary assessment	
Different dietary assessment methods	+/-
Measurement uncertainty in the concentrations analysed	+/-
Bias due to misreporting	+/-
Use of upper bound (UB) in exposure assessment	+
Use of lower bound (LB) in exposure assessment	-
Data for cod has been used for lean fish content in all types of fish products	+/-
Småbarnskost 2007	
Use of 95 th percentile	+/-
Food frequency questionnaire (FFQ) time span is 14 days	+/-
Norkost 3, Adults	
Low participation rate (selection bias)	+/-
Two registration days	+
Use of 95 th percentile	+
MoBa, pregnant women	
Low participation rate (40.6% of those invited) (selection bias)	+/-
Recall 4-5 months back in time and possible misreporting of consumption (recall bias)	+/-

Source of uncertainty	Direction
Epidemiological studies	
Inclusion and exclusion criteria	+/-
Definition of fish consumption frequency and the exposure e.g. types of fish	+/-
Variation of contaminant levels in the same fish species	+/-
Confounding factors	+/-
Nutrients and contaminants in fish	
Annual variation (especially for small sample sizes)	+/-
Small number of samples for some fish species	+/-
Sampling methods and representativity	+/-
Precision of analytical methods	+/-
Nutrients and contaminants analysed in raw fish	+/-
Fish feed	
Small number of samples for some years	+/-
Sampling methods and representativity	+/-
Precision of analytical methods	+/-

+ : uncertainty likely to cause over-estimation of exposure.

- : uncertainty likely to cause under-estimation of exposure.

Despite some limitations in assessing the fish consumption and the uncertainties related to the estimated intakes of nutrients and exposures to contaminants from fish and fish products, VKM concludes that the intake and exposure estimates presented in this opinion are within realistic ranges for each study population.

VKM compared intakes of nutrients with national recommended intake values and exposures to contaminants with internationally recognised health based guidance values (tolerable weekly intakes - TWIs). Likewise, the benefits for health associated with fish consumption were also evaluated by international bodies, and the uncertainties in these assessments were not evaluated by VKM. VKM considers the overall uncertainty in the outcome of the present assessment on benefit and risk of fish consumption in Norway to be low.

10 Answers to the terms of reference

The Norwegian Food Safety Authority (NFSA) requests an update of the benefit risk assessment published by VKM in 2006, "A comprehensive assessment of fish and other seafood in the Norwegian diet". VKM is requested to base the updated assessment on new knowledge about fish, and farmed fish in particular. Furthermore, VKM is requested to focus on levels of specific nutrients, (n-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), vitamin D, iodine and selenium) and specific contaminants (dioxin and dioxin-like PCBs, mercury) in fish fillet for impact of positive and negative health effects of fish consumption, respectively.

VKM has the following answers to the questions in the terms of reference (ToR):

ToR 1: What are the main changes in the use of raw materials in feed, and how are these changes reflected in the levels of nutrients, dioxins and dioxin-like PCBs and mercury?

Since 2006 the production volume of farmed Atlantic salmon and trout has increased dramatically followed by increased requirement for feed volume. During the same period fish meal and fish oil available for feed production have remained constant. Hence, new raw materials have increasingly replaced fish meal as protein source and fish oil as lipid source. Thus, over the last 10 years there has been a great change in raw materials used in fish feeds, and in 2013 terrestrial plant proteins and vegetable oils accounted for 70% of the feed. In 2013, vegetable oil (mainly as rapeseed oil) constitutes approximately 64% of the feed oil.

Main changes in the levels of nutrients: Replacing fish oil with vegetable oils in fish feed results in increased content of the long-chain polyunsaturated fatty acids (PUFAs) from terrestrial plants, n-6 PUFAs (linoleic acid (LA) and alpha-linolenic acid (ALA), and decreased content of PUFAs of marine origin, n-3 LCPUFAs (eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and docosapentaenoic acid (DPA). Comparable data on fish feed levels of EPA, DHA and n-6 PUFAs in 2006 and 2014 are not available. Furthermore, VKM states that for vitamin D, selenium and iodine the change in raw materials for use in fish feed since 2006 has resulted in 36, 45, and 50% decreases, respectively, of the corresponding feed levels in 2014.

Main changes in levels of contaminants in fish feed: The change in inclusion levels of fish oil from early 2000 has also affected the levels of persistent organic pollutants (POPs) in fish feed, and the level of dioxins and dl-PCBs is reduced by almost 60% in 2013 compared to 2006. Mercury levels have also decreased by approximately 50% in feed for Atlantic salmon and rainbow trout since 2006 due to the increasing fishmeal replacement with terrestrial plant protein sources. For details see Chapter 5.

ToR 2: To what extent have levels of nutrients and contaminants in fish changed since 2006? Describe this change.

There is no difference in amino acid composition when comparing fillet of farmed Atlantic salmon from 2006 and 2014, since irrespective of which raw material that provides the dietary amino acids the fish muscle protein composition remains the same.

The change in concentrations of nutrients and contaminants in fish feed for farmed Atlantic salmon and trout due to replacement of fish oil and fish protein with plant proteins and vegetable oils, is reflected in changed concentration and composition of the same nutrients and contaminants in the farmed fish fillet. The major changes are that the concentrations of EPA+DHA and selenium have decreased about 50 and 60%, respectively since 2006, and that concentrations of dioxins and dl-PCBs have been reduced by almost 70% and mercury by about 50% in the current report compared to the VKM report from 2006.

For wild caught fish species the composition of nutrient and contaminant composition of the diet is also reflected in the edible part of the fish. The available databases of nutrient and contaminant concentrations for wild caught fish are not suitable to reveal time-trends of nutrient and contaminant levels, however there seem to be minor or no changes of the composition and concentrations of nutrients and contaminants in wild caught fish since 2006. For details see Chapter 5.

ToR 3: Calculate the intake and exposure of these substances (nutrients and contaminants) on the basis of recent dietary data.

Since 2006, the data bases on both nutrient and contaminant concentrations in both wild and farmed fish have been improved substantially and updated information on fish consumption in 2-year-olds (conducted in 2007), adults (conducted in 2010-2011, 18-70 years of age) and pregnant women (conducted in 2002-2008) has become available. The expanded databases reduce the uncertainties in the intake and exposure estimates of nutrients and contaminants, respectively, in 2014 compared to 2006. For details see Chapters 3, 6 and 7.

Nutrient intake estimates: Current nutrient intakes for 2-year-olds, adults (18-70) and pregnant women have been calculated from fish consumption data derived from the respective food consumption surveys and data on nutrient levels in the fish/fish product consumed.

EPA, DPA and DHA

The main source is fatty fish, besides fish oil and cod liver oil which is consumed by a relative large part of the populations (41% of the 2-year-olds, 37% of the adults and 77% for pregnant women). In **2-year-olds**, the mean intake of EPA+DHA+DPA contributed by fish is 204 mg/day. In **adults**, the amount of EPA+DPA+DHA from mean total fish intake is approximately 500 mg/day, and the 95th percentile is 2132 mg/day which is an overestimate. In **pregnant women**, the mean estimated intake of EPA+DHA+DPA is 312 mg/day, and the 95th percentile is 992 mg/day.

Vitamin D

The main source for vitamin D is fatty fish, besides fish oil and cod liver oil which is consumed by a relatively large part of the populations (41% of the 2-year-olds, 37% of the adults and 77% of pregnant women). Vitamin D contributed by fish in **2-year-olds** and **adults** are on average 0.36 and 2.1 µg/day, respectively. In **pregnant women**, the mean vitamin D intake from fish is 0.96 µg/day.

Iodine

Lean fish is the main source for iodine. In **2-year-olds** average fish consumption contributes with 35 µg iodine per day. The mean intake of iodine from fish in **adults** is 86 µg iodine per day and in **pregnant women** 54 µg.

Selenium

The selenium concentration is about the same in lean and fatty fish. In **2-year-olds**, the contribution of selenium from average fish consumption is 4.5 µg/day. In **adults**, the mean selenium intake from fish is 15 µg/day and in **pregnant women** 9 µg/day.

Contaminant exposure estimates: Current exposure estimates for 2-year-olds, adults (18-70 years) and pregnant women have been calculated from fish consumption data derived from the respective food consumption surveys and data on contaminants levels in the fish/fish product consumed.

The exposure to mercury and dioxins and dl-PCBs through fish consumption has been given both in upper bound (UB) and lower bound (LB). In UB calculations the concentrations lower than the limit of quantification (LOQ) or limit of detection (LOD) is substituted with the LOQ or LOD. This most likely represents an overestimate of the exposure. In LB calculations, concentrations lower than the LOQ or LOD is substituted with 0. This most likely represents an underestimate of the exposure. For mercury there are small differences between lower bound and upper bound estimates because concentrations in most samples have been quantified. Therefore, the description on mercury exposure in the text is based on UB estimates. For dioxins and dl-PCBs the uncertainty in concentrations in fish is higher and in order to reflect this, both UB and LB results are described also in the text.

Methylmercury

For methylmercury exposure, fish is the only notable source. Methylmercury constitutes 80-100% of the total mercury in fish. The main source in Norway is lean fish.

The updated UB exposure assessments indicated mean and 95th percentile exposure in **2-year-old** at 0.50 and 1.1 µg/kg bw/week. In **adults**, the mean and 95th percentile exposures were 0.30 and 1.2 µg/kg bw/week, and in **pregnant women** the mean and 95th percentile exposures were 0.17 and 0.39 µg/kg bw/week, respectively. For mercury exposure from fish, the upper and lower bounds are quite similar.

Dioxins and dl-PCBs

Fatty fish is the major contributor, but consumption of cod liver oil may contribute in addition. In adults, cod liver oil contributes a smaller part, whereas cod liver oil constitutes a larger part in 2-year-olds. The updated exposure assessments from fish indicates mean exposure in **2-year-olds** between 2.0 (LB) and 2.6 (UB) pg TEQ/kg bw/week and 95th percentile exposure between 7.3 (LB) and 9.4 (UB) pg TEQ/kg bw/week. In **adults**, the mean exposure was between 1.4 (LB) and 1.7 (UB) pg TEQ/kg bw/week and the the 95th percentile exposure was between 5.6 (LB) and 6.8 (UB) pg TEQ/kg bw/week. In **pregnant women**, the mean exposure was between 0.75 (LB) and 0.94 (UB) pg TEQ/kg bw/week and the 95th percentile exposure was between 2.2 (LB) and 2.7 (UB) pg TEQ/kg bw/week.

Changes in nutrient intake and contaminant exposure since 2006: The updated **nutrient** calculations in the current opinion indicate no change in EPA+DPA+DPA contributed by fish consumption, a modest decline in the amount of vitamin D contributed by fish, and a substantial decline in iodine and selenium. There is no environmental or biological reason why iodine and selenium intake from fish should be decreased since 2006, as long as the fish consumption is unchanged. The observed differences are likely due to improved data on iodine and selenium concentrations in wild fish in 2014 and thus less uncertainty now than in the intake assessments in 2006.

The main difference regarding **mercury** exposure from fish is that the database on mercury concentrations in fish has been substantially improved since the assessment in 2006, and this has reduced the uncertainties in the exposure estimates. Overall, the exposure estimates for mercury from fish in 2006 and 2014 are similar.

Also for **dioxins and dl-PCBs** the database on concentrations in fish has improved substantially since the assessment in 2006, reducing the uncertainty in the exposure assessments. There is a decreasing trend of dioxins and dl-PCBs in the environment and therefore also in food. A decrease in exposure to dioxins and dl-PCBs from fish can be seen since 2006, as present exposure is estimated to be around 40% of the exposure calculated in 2006. The decrease is likely due to a combination of more data on levels of dioxins and dl-PCBs in fish in 2014 than in 2006, and decreased levels of dioxins and dl-PCBs in the environment, as well as in farmed salmon. The reduced level of dioxins and dl-PCBs in

farmed fish is mainly due to decreased fish oil inclusion in fish feed today compared to 2006. In contrast to farmed fish, the available data for wild fish are not suitable to show time-trends of contaminant levels e.g. regular sampling of the same species from the same area over a long period of time.

ToR 4: Consider the benefits of eating fish with regard to the intake of nutrients and the risks associated with the intake of dioxins, dioxin-like PCBs and mercury.

The present benefit-risk assessment is comprised of three elements, i.e. risk assessment, benefit assessment and benefit-risk comparison (Chapter 8).

Fish consumption and association with health outcomes

Since 2006 large prospective cohort and population studies have been conducted assessing fish consumption and associations with different health outcomes. VKM has summarized research on association between fish consumption and several health effects (cardiac disease, neurodevelopment and other outcomes related to the central nervous system, cancer, type-2 diabetes and other metabolic outcomes, asthma, allergy and other atopic outcomes, and pregnancy-related outcomes). A comprehensive summary of health effects associated with fish consumption is given in Chapter 4.8.

VKM concludes that meta-analyses conducted since 2009 do not show association between fish consumption and **cancer**. Furthermore, the studies summarized have not revealed consistent associations between fish consumption and **type-2 diabetes**, although some Nordic studies indicate protective associations. None of the studies controlled for contaminant exposure from fish, and it is not known whether this would have affected the outcome.

No meta-analyses reported association between fish consumption and adverse health effects. A few studies showing positive health effects of fish consumption reported a decrease in the positive health effects by contaminants in fish (negative confounding).

Beneficial effects of fish consumption: VKM is of the opinion that according to epidemiological studies, the net effects of the present average fish consumption in Norway for adults including pregnant women is beneficial for specific cardiovascular diseases (particularly cardiac mortality, but also with regard to ischaemic stroke, non-fatal coronary heart disease events, congestive heart failure and atrial fibrillation) as well as for optimal neurodevelopment for foetuses and infants. VKM notes that the calculated benefits of fish consumption in relation to the health outcomes mentioned above refer to net effects combining beneficial, neutral, and adverse effects of nutrients and non-nutrients, including contaminants such as methylmercury, dioxins, dl-PCBs. VKM also notes that EPA and DHA play a role. However, the beneficial effects of fish intake are most likely mediated through a complex interplay among a wide range of nutrients commonly found in fish, thus fatty and/or

lean fish may be involved. VKM is of the opinion that adults including pregnant women with fish consumption less than one dinner serving per week may miss the beneficial effects on cardiovascular diseases and optimal neurodevelopment of foetus and infant. The health benefit of fish consumption is reported from 1-2 dinner servings per week and up to 3-4 dinner servings per week. The health benefit of fish consumption is reported from 1-2 dinner servings per week and up to 3-4 dinner servings per week. For higher fish intake per week the limited number of consumers in epidemiological studies does not allow for drawing firm conclusions about the actual balance of risk and benefit. More knowledge is needed to reveal the beneficial mechanisms of fish consumption.

Furthermore, for pregnancy-related outcomes, VKM notes that results from MoBa indicate that fish consumption during pregnancy, and in particular lean fish consumption is associated with increased birth weight and lower risk of preterm birth, however, the findings need to be confirmed in other cohorts. Regarding atopic diseases, VKM also notes that results from MoBa indicate a protective association between maternal fish consumption and/or early life fish consumption and atopic diseases. None of the studies controlled for contaminant exposure from fish and it is not known whether this would have affected the outcome.

Benefit characterisation of nutrients in fish: VKM has estimated the contribution from fish to the recommended intakes of certain nutrients. Fish is the major source of EPA+DPA+DHA, but for vitamin D, iodine and selenium there are also other substantial sources. Fish is not a major dietary source of n-6 fatty acids, also not when the consequences of inclusion of plant oils in the feed for farmed Atlantic salmon have been taken into consideration in the intake assessments. Based on intake estimates in comparison with upper limits of nutrients, it is unlikely that fish consumption in Norway could lead to harmful high intake of vitamins, minerals or n-3 LCPUFAs for any age group. Therefore, in the present assessment of nutrients VKM focuses on the possible benefits of intake of nutrients from fish consumption in relation to recommended nutrient intakes.

Taking the current levels of nutrients in fish, and the consumption of fish in different population groups in Norway into account, VKM concludes that the contribution of **EPA+DHA** from average fish consumption will reach the European recommended intake of EPA+DHA for adults and 2-year-olds. For pregnant women the average fish consumption is insufficient to meet the European recommendation of EPA and DHA for pregnant women, but sufficient to meet the national intake recommendation of DHA. With high fish consumption (95th percentile), all age groups will reach the recommended intake of EPA and DHA.

For **vitamin D**, current average fish consumption contributes approximately to 1/5 of the recommended intakes for adults but less for pregnant women and 2-year-olds. Since there are few other dietary vitamin D sources, this supports the necessity for the current recommendation of vitamin D supplements in the population.

Fish contributes with 30 to 50% (mean fish consumption in adult and pregnant) and up to 90% (mean fish consumption in 2-year-olds) of the recommended **iodine** intakes for the different age groups. High fish consumption contributes with 48% of the recommended

selenium intake for 2-year-olds and less for adults and pregnant women. Low intakes of **selenium and iodine** from fish relative to the recommended values may be complemented by intake from other dietary sources.

Risk characterisation of undesirable substances in fish: VKM has compared the dietary exposure to contaminants contributed by fish with the tolerable weekly intakes. A tolerable intake is the amount of a substance, or substance group, which can be consumed safely throughout a person's lifetime without appreciable risk of adverse health effects. Tolerable intakes are set by international risk assessment bodies, such as WHO or EFSA, and incorporate safety margins, in order to protect all parts of the population.

VKM concludes that with the present mean concentration of **mercury** in fish on the Norwegian market and the present fish consumption in Norway, the methylmercury exposure from fish is below the tolerable weekly intake (TWI) of 1.3 µg/kg bw/week for more than 95% of the population of 2-year-olds, adults and pregnant women. This exposure represents a negligible risk and is of no concern.

With the present mean level of **dioxins and dl-PCBs** in fish on the Norwegian market and the present fish consumption in Norway, high fish consumption (the 95th percentile) contributes with up to 50%, 19%, 67% of the TWI of 14 pg TEQ/kg bw/week for adults, pregnant women and 2-year-olds respectively. Daily consumption of cod liver oil or fish oil (which is common in all population groups) in amounts as suggested on the product will in addition contribute with 0.8 to 16% of the TWI, depending on the body weight. With the present TWI and taking into consideration that fish and fish products are significant sources to dioxins and dl-PCBs in the Norwegian diet, VKM concludes that the exposure from fish to dioxins and dl-PCBs represents negligible risk and is of no concern.

Scenarios: VKM has made various scenarios to foresee how possible changes in fish consumption pattern and amounts will affect the exposure from fish to tolerable weekly intakes of mercury, dioxins and dl-PCBs. Fish is the only source for methylmercury exposure from foods, whereas exposure to dioxins and dl-PCBs also comes from other foods than fish.

Based on these scenarios, where only exposure to dioxins and dl-PCBs from fish were taken into consideration, VKM is of the opinion that fish consumption in line with the food-based dietary guideline of 300-450 g fish, hereof 200 g fatty fish per week, does not lead to exposures to dioxins and dl-PCBs or methylmercury from either fatty or lean fish exceeding the respective TWIs, and is therefore, from a contaminant exposure perspective, of no concern.

However, since there are other food sources in the Norwegian diet that contribute to exposure to these contaminants, VKM performed a simple model estimate of weekly intake of dioxins and dl-PCBs in adults from various amounts of farmed salmon and other foods. Based on this scenario, VKM is of the opinion that there is negligible risk associated with eating farmed Atlantic salmon with the present mean concentrations of dioxins and dl-PCBs. The TWI is not exceeded when consuming amounts equivalent to 1400 g farmed salmon

weekly for adults (representing 9 weekly dinner servings). Neither is the TWI exceeded when exposures to dioxins and dl-PCBs from other foods and cod liver oil are taken into consideration. In comparison, an adult can consume about 800 g mackerel weekly (representing 5 weekly dinner servings) with current mean concentration of dioxins and dl-PCBs without exceeding TWI. From a contaminant exposure perspective consumption of farmed salmon is of no concern. This also applies for commercially available wild caught fish like mackerel.

VKM is of the opinion that the present exposure to residues of veterinary medicinal products including **residues of antibiotics** in farmed fish in the Norwegian diet is of no concern since the levels are very low and often not detectable even with sensitive analytical methods.

For new contaminants in fish feed like the **pesticide endosulfan, polyaromatic hydrocarbon (PAHs) and mycotoxins**, VKM is of the opinion that the concentrations in farmed fish in the Norwegian diet are likely not a food safety issue since the concentrations are very low and often not detectable even with sensitive analytical methods.

Regarding the environmental contaminants **brominated flame retardants**, VKM refers to the conclusions in a risk assessments from EFSA in 2011 that the health risk associated with the current exposure to these compounds is low. The amount of **fluorinated compounds** such as PFOS and PFOA in the Norwegian diet is much lower than what is tolerable according to an EFSA assessment in 2008.

Benefit-risk comparison

From **a benefit assessment perspective**, VKM is of the opinion that the average fish consumption in Norway for adults should give substantial benefit (positive health effects) with regard to specific cardiovascular disease. Pregnant women, who eat little or no fish, may miss the beneficial effects of fish consumption on neurodevelopmental outcomes in foetuses and infants.

From **a nutrient benefit assessment perspective**, VKM is of the opinion that for the different age groups, increase in both lean and fatty fish consumption will improve the role of fish as a source of important nutrients (EPA+DPA+DHA, vitamin D, iodine and selenium) relative to recommended intakes. Increased consumption of fatty fish will increase the intake of EPA+DPA+DHA and vitamin D while an increase in the consumption of lean fish will increase the intake of iodine. Generally, an increase of marine fish consumption will increase the intake of selenium.

From **a risk perspective** it is the opinion of VKM that with the present concentrations of dioxins and dl-PCBs, and mercury, the exposure to these compounds is below the tolerable intakes when fish is consumed in accordance with the dietary advice of 300-450 g fish per week (representing 2-3 dinner servings, hereof 200 g fatty fish), and is therefore of no concern. This also apply if the fish consumed in adults consist of 1400 g farmed Atlantic

salmon (representing 9 dinner servings) or 800 g mackerel weekly (representing 5 dinner servings).

Following a comprehensive assessment of the scientific literature on the positive health effects of fish consumption and the contribution from fish to intake of beneficial compounds as well as exposure to hazardous contaminants in Norway, VKM concludes that the benefits clearly outweighs the negligible risk presented by current levels of contaminants and other known undesirable substances in fish. Furthermore, in Norway, adults including pregnant women with fish consumption less than one serving per week may miss the beneficial effects on cardiovascular diseases and optimal neurodevelopment in foetuses and infants. In contrast to the conclusion in 2006, VKM concludes that there is no reason for specific dietary limitations on fatty fish consumption for pregnant women.

The health benefit of fish consumption is reported from 1-2 dinner servings per week and up to 3-4 dinner servings per week. For higher fish intake per week, the limited number of consumers in epidemiological studies does not allow for drawing firm conclusions about the actual balance of risk and benefit. More knowledge is needed to reveal the beneficial mechanisms of fish consumption.

ToR 5: Does this change the conclusions from the report in 2006?

Fish consumption and dietary guidelines

Existing dietary guidelines: In 2006, the Norwegian recommendation for fish consumption merely was to eat more fish both for dinner and as bread spreads. In 2014, based on the VKM assessment in 2006 (VKM, 2006) and the report "Dietary advice to promote public health and prevent chronic diseases in Norway" (Norwegian National Council for Nutrition, 2011), these recommendations were altered and made quantitative by the Norwegian Directorate of Health (2014). The Norwegian Directorate for Health now (per 2014) recommends fish as dinner meal 2-3 times per week for all age groups. Fish is also recommended as bread spread. This represents totally 300-450 g fish per week for adults, and less for children. For adults, at least 200 g should be fatty fish such as salmon, trout, mackerel or herring. Six portions of bread spreads represents approximately one dinner portion. A clarification was given for young females and pregnant women. They should, over time, avoid eating more than two meals of fatty fish per week, including fish like salmon, trout, mackerel and herring. The Norwegian health authorities also recommend a daily supplement of vitamin D to infants from 4 weeks of age, and if this supplement is taken as cod liver oil it will in addition ensure an adequate supply of n-3 LCPUFAs (Chapter 1).

Current fish consumption: Fish consumption of 2-year-olds, adults (18-70 year of age) and pregnant women have been calculated from the food consumption surveys Småbarnskost 2007 (n=1674), Norkost 3 (n=1787) and MoBa (n=83 848), respectively. According to these estimates adults eat on average 364 g/week (equivalent to 2-3 fish

dinner servings per week given a portion size of 150 g), pregnant women eat 217 g/week (equivalent to 1-2 dinner servings per week given a portion size of 150 g), while 2-year-olds eat 112 g/week (equivalent to 1-2 dinner servings per week given a portion size of 75 g) (see Chapters 3 and 8 for details).

Comparison of fish consumption and food based dietary guidelines: VKM concludes that of the different population groups, only adults (18-70 years of age) with an average or higher fish consumption reach the food based dietary guidelines for total fish consumption. Both the mean total and fatty fish consumption of children (2-year-olds) and pregnant women as well as the mean fatty fish consumption of adults are lower than recommended. A larger proportion of the pregnant women compared to other adults have fish consumption less than the recommendations.

Comparison of conclusions in 2006 and 2014: In 2006, exposure to dioxins and dl-PCBs exceeded the tolerable intake for approximately 15% of the population. In the present benefit-risk assessment VKM concludes that for all population groups studied (2-year-olds, pregnant women and adults), the exposure to dioxins, dl-PCBs and mercury is below the tolerable intakes with the present fish consumption. This would be the case also if fish is consumed in accordance with the dietary advice of 300-450 g fish hereof 200 g fatty fish per week (representing 2-3 dinner servings). Furthermore, based on scenarios VKM is of the opinion that this also apply if the fish consumed in adults consist of 1400 g farmed Atlantic salmon (representing 9 dinner servings) or 800 g mackerel weekly (representing 5 dinner servings). VKM is of the opinion that from a contaminant exposure perspective consumption of farmed salmon is of no concern. This also applies for commercially available wild caught fish like mackerel. In the 2006 report, it was concluded based on the levels of contaminants in farmed salmon, "Over a long period of time, eating more than 2 meals of fatty fish per week at current levels of dioxins and PCBs may result in the tolerable intake (TWI) for dioxins and dioxin-like PCBs being moderately exceeded. This is especially important with respect to fertile women". In contrast to the cited conclusion of 2006, VKM concludes in this report that there is no reason for specific dietary limitations on fatty fish consumption for pregnant women.

Health effect of fish consumption

Beneficial health effects of fish consumption: In the present VKM report, literature addressing fish consumption and effects on specific health outcomes that was considered relevant for the benefit-risk evaluation has been reviewed. This includes systematic reviews and meta-analyses, assessments prepared by international scientific bodies as well as some single cohort or population-based studies published after 2006. It appears that of the assessed health endpoints, there are more studies and more evidence related to fish consumption and cardiovascular endpoints and neurodevelopment, than for the other assessed endpoints (cancer, type-2 diabetes and other metabolic outcomes, asthma, allergy, and other atopic diseases, pregnancy-related outcomes, neurodevelopment, and cognitive decline, including Alzheimers disease). VKM concludes that documentation of the benefits of

fish consumption in relation to cardiovascular diseases and mortality as well as neurodevelopment of foetus and infant has been strengthened since 2006. VKM notes that the benefits of fish consumption refer to net effects combining beneficial, neutral, and adverse effects of nutrients and non-nutrients (including contaminants such as methylmercury, dioxins and dl-PCBs) in fish. VKM also notes that EPA and DHA from fish play a role, however, the beneficial effects of fish consumption most likely are mediated through a complex interplay among a wide range of nutrients commonly found in fish, thus fatty and/or lean fish may be involved.

ToR 6: On the basis of updated knowledge, please comment if other substances, like pesticide and drug residues, which are not listed, could affect the conclusions with regard to the impact on public health?

All feed ingredients may contribute with undesirable substances. Replacing fish oil and fish meal with alternative ingredients decreases the levels of marine contaminants, however, the new ingredients may contribute with similar and/or other types of contaminants.

For new contaminants in fish feed like the pesticide endosulfan, polycyclic aromatic hydrocarbons (PAH) and mycotoxins, VKM is of the opinion that the reported concentrations in farmed fish in the Norwegian diet is not likely a food safety issue since the concentrations are very low and often not detectable even with sensitive analytical methods.

With regard to the synthetic antioxidants (ethoxyquin, butylhydroksyanisol (BHA) and butylhydroksytoluen (BHT)) and the pesticide endosulfan, the calculated exposures from a 300 g portion of farmed fish fillets are reported to be below their respective acceptable daily intakes (ADIs) and therefore of no concern.

The concentrations of brominated flame retardants and perfluorated organic compounds in fish feed and fish on the Norwegian market are generally low, and considered to be of no concern from a human health perspective by VKM.

VKM is of the opinion that the present exposure to residues of veterinary medicinal products including residues of antibiotics in farmed fish in the Norwegian diet is of no concern since the reported concentrations are below maximum residue limits (MRLs) for the respective active substances.

11 Data gaps

No essential data gaps have been identified for conducting this benefit-risk assessment of fish and fish products in the Norwegian diet. However, during preparation of the present report, it is revealed that future benefit-risk assessment of fish consumption will profit from enlargement of data on nutrient composition and content in wild and farmed fish and in commercial available fish based products. In order to show time-trends of both nutrients and contaminant levels in wild caught fish, regular sampling of the same species from the same area over a long period of time is of importance. For farmed fish, changes in fish feed recipe should be followed by continuing scientific research and monitoring to reveal its impact on fish as food. In order to follow changing trends in food consumption in the Norwegian population, regular conduction of national dietary surveys in all age groups is important. Some of the abovementioned areas are detailed below:

- There is a lack of data on nutrients and contaminants in commercial products containing fish like fish cakes and bread spreads, ready to eat meals (fish soup and fish au gratin). Knowledge of concentrations of nutrients and contaminants in these products will refine the intake and exposure calculations.
- There are no available samples suitable to show time-trend of contaminant levels in wild fish, such as regular sampling of the same species, e.g. cod liver and fillet, from the same area over a long period of time. Such data is only available for farmed fish.
- Data from the national food dietary surveys among children and adolescents (i.e. 4-, 9-, and 13-year-olds), conducted in 2000 and 2001, were considered too old to be used in this opinion. It is of importance that the national dietary surveys in all age groups are conducted regularly to follow the changing trends in food consumption, at least each 5th-10th year.
- The relevance and challenges of a two times 24h-recall dietary method as used in Norkost 3 for use in intake/exposure assessment should be further clarified
- More knowlegde is needed to reveal the beneficial mechanisms of fish consumption.
- There is a need for studies assessing health effects of fish consumption that control for potential effects of concomitant contaminants exposure.
- Changes in fish feed recipe and the subsequent impact on fish as food needs to be followed
 - Plant ingredients used in fish feed may introduce new contaminants such as PAHs, mycotoxins, and new pesticides. More knowledge are needed on the concentrations in fish feed and transfer from feed to fish fillet of new

contaminants as well as for the brominated flame retardants and perfluorated compounds.

- Future new feed ingredients, including GM-oils and protein sources, for farmed fish feed introduce contaminants as well as nutrients. When future new ingredients are introduced, knowledge on nutrient and contaminant composition, content, impact on fish health and if they affect the eatable portion and its consumer, is needed.

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Appendix I

Fish species and percentage raw fish used for each fish product in calculations of fish consumption for 2-year-olds, pregnant women and adults

Fish consumption from national dietary surveys among 2-year-olds (Småbarnskost 2007) and adults (Norkost 3) as well as information about fish consumption reported during the time period 2002-2008 by pregnant women in Norwegian Mother and Child Cohort Study (MoBa), are described in Chapter 3. The fish consumption is presented as raw fish to match the concentration data of nutrients and contaminants analysed in raw fish. Details regarding percentages of raw fish in various fish products, and for the fish species used for each fish product, are presented below in Tables AI-1, AI-2 and AI-3.

Table AI-1 Type of fish and percentage of raw fish in fish products used in calculations in the Småbarnskost 2007 study for fish consumption in 2-year-olds

Fish/fish product	Percent of raw fish in the product's recipe (%)	Fish species used for consumption calculations
Cod, saithe, other white fish (as dinner)	100	Atlantic cod
Trout, salmon, mackerel, herring (as dinner)	100	Atlantic salmon (farmed)
Fish balls, fish pudding	55	Atlantic cod
Fish au gratin	50	Atlantic cod
Fish burgers	60	Atlantic cod
Fish fingers	60	Atlantic cod
Jarred baby food with fish	10	Atlantic cod
Mackerel in tomato-sauce	60	Mackerel (North East Atlantic)
Caviar	46	Atlantic cod roe

Table AI-2 Type of fish and percentage of raw fish in fish products, used in calculations for in the Norkost 3 study for fish consumption in adults

Fish/fish product	Percent of raw fish in the product's recipe (%)	Fish species used for consumption calculations
Salmon, trout	100	Atlantic salmon (farmed)
Farmed trout	100	Atlantic salmon (farmed)
"Klippfisk"	200	Atlantic cod
"Bokna fish"	111	Atlantic cod
"Lutefisk"	61	Atlantic cod
Fish pudding*	55	Atlantic cod
Fish balls*	55	Atlantic cod
Fish cakes*	60	Atlantic cod

Fish/fish product	Percent of raw fish in the product's recipe (%)	Fish species used for consumption calculations
Salmon cakes	83	Atlantic salmon (farmed)
Fried breaded saithe	70	Saithe
Fried breaded cod	60	Atlantic cod
Fried breaded plaice	70	Plaice
Mackerel in tomato sauce	60	Mackerel (North East Atlantic)
Sushi	33	Atlantic salmon (farmed)
Fish au gratin*	50	Atlantic cod
Crab sticks*	72	Atlantic cod
Pickled herring	60	Herring (Norwegian spring spawning)
Caviar	46	Atlantic cod roe
Caviar light	68	Atlantic cod roe
Caviar mix	27	Atlantic cod roe
Fish soup	20	Atlantic salmon (farmed)

* white fish is a common source of fish in many fish products in Norway, however, due to lack of data for white fish the nutrient content of cod is used in the calculations.

Table AI-3 Type of fish and percentage of raw fish in fish products used in calculations for the MoBa study for fish consumption in pregnant women

Fish /fish product	Percent of raw fish in the product's recipe (%)	Fish species used for consumption calculations
Cod, saithe	100	Atlantic cod
Pike, perch	100	Pike
Mackerel, herring	100	Mackerel (North East Atlantic)
Salmon, trout	100	Atlantic salmon (farmed)
Fish products like fish pudding, fish balls, fish burgers	60	Atlantic cod
Fish pate	50	Atlantic salmon (farmed), Atlantic cod
Fried breaded fish	67	Atlantic salmon (farmed), Atlantic cod
Pasta dish with fish	20	Atlantic cod
Mackerel in tomato-sauce	60	Mackerel (North East Atlantic)
Caviar	60	Atlantic cod roe

Appendix II

List of fish species and fish based products named in English, Norwegian and Latin (if relevant)

Table AII-1 Fish species and fish based products listed alphabetically in English, Norwegian and Latin

English fish name	Norwegian fish name	Latin fish name
Atlantic cod, all populations	Torsk (alle typer)	<i>Gadus morhua</i>
Cod (costal)	Kysttorsk	-
Cod (North Sea)	Nordsjøtorsk	-
Cod (North East Atlantic)	Nordøstatlantisk torsk	-
Atlantic halibut	Kveite	<i>Hippoglossus hippoglossus</i>
Atlantic salmon (wild)	Villaks	<i>Salmon salar</i>
Atlantic salmon (farmed)	Oppdrettslaks	<i>Salmo salar</i>
Arctic char (farmed)	Oppdrettsrøye	<i>Salvelinus alpinus</i>
Brown trout	Ferskvannsrørret	<i>Salmo trutta</i>
Cod roe	Torskerogn	-
Cod roe and liver pate	Svolværpostei	-
Fish liver	Fiskelever	-
Greenland halibut	Blåkveite	<i>Reinhardtius hipoglossoides</i>
Haddock	Hyse	<i>Melanogrammus aeglefinus</i>
Herring (North Sea herring)	Nordsjøsil	<i>Clupea harengus</i>
Herring, (Norwegian spring spawning)	Norsk vårgytende sil	<i>Clupea harengus</i>
Mackerel (North East Atlantic)	Nordøstatlantisk makrell	<i>Scomber scombrus</i>
Perch	Abbor	<i>Perca fluviatilis</i>
Pike	Gjedde	<i>Esox lucius</i>
Plaice	Rødspette	<i>Pleuronectes platessa</i>
Redfish	Uer	<i>Sebastes marinus</i>
Saithe	Sei	<i>Pollachius virens</i>
Sprat	Brisling (hel og fersk)	<i>Sprattus sprattus</i>
Mackerel in tomato sauce	Makrell i tomat på boks	-
Trout (farmed)	Oppdrettsørret	<i>Onocorhynchus mykiss</i>
Tuna (canned)	Tunfisk på boks (Tunfisk på boks er ofte bukstripet bonitt, <i>Katsuwonus pelamis</i>)	<i>Thannus</i> (Canned tuna is often based on <i>Katsuwonus pelamis</i>)
Wolffish	Gråsteinbit	<i>Anarhichas lupus</i>

Appendix III

Differences in dietary assessment methods used by VKM in 2006 and 2014 - details

In order to address changes in fish consumption since 2006, the methods behind the dietary surveys used then and now have been taken into consideration; see Chapter 3 in the main text.

The method used for consumption recording in Småbarnskost 1999 and Småbarnskost 2007 were similar (food frequency questionnaire; FFQ), and data from these two surveys can be compared even though the questions in the FFQs differ for some food groups (see Chapter 3.3). However, for adults, the methods used in the Norwegian Fish and Game study (FFQ) and in Norkost 3 (24-hour recalls), respectively, are **not** similar, and data from these two surveys cannot be directly compared. However, both studies were nation-wide and participants were invited by arbitrary selection from the population. The Norwegian Mother and Child Cohort Study (MoBa) is a prospective population-based pregnancy cohort study which among other issues addresses the dietary habits during the first 4-5 months of pregnancy.

Details of changes in the methods used for dietary assessment in 2006 and 2014 are outlined in Table AIII-1.

Table AIII-1 Changes in the dietary assessment methods used in the 2006 and the present benefit-risk assessment of fish

Population groups	Dietary assessment survey		Methods used		Number of questions on fish consumption	
	2006	2014	2006	2014	2006	2014
2-year-olds	Småbarnskost 1999 Food frequency questionnaire	Småbarnskost 2007 Food frequency questionnaire	Frequency range after 'never/less than once per month' Seldom to often	Frequency range after 'never/less than once per month' Seldom to often	7	10
Adults	The Norwegian Fish and Game study Part A Food frequency questionnaire	Norkost 3 24-hour recalls	Closed long term method	Open short term method	26 on fish/shellfish for dinner, 1 on fish as bread spread	Open, 97 different fish and fish containing foods reported
Pregnant women	MoBa 2006 (preliminary data) Food frequency questionnaire	MoBa 2008 (complete) Food frequency questionnaire	Closed long term method	Closed long term method	16 on fish/shellfish for dinner, 10 on fish/shellfish as bread spread, 4 on cod liver oil and fish oil	16 on fish/shellfish for dinner, 10 on fish/shellfish as bread spread, 4 on cod liver oil and fish oil

Appendix IV

Search terms for fish consumption and health outcomes

This Appendix refers to Chapter 4 “Health effects associated with fish consumption – epidemiological studies” in the main text.

The search was performed 11. April 2014. For the main search (Table AIV-1), fish consumption was combined with one or several health outcomes, language was English or Scandinavian, human studies only was included and publication date was from 2009 until day of searching. The number of hits was 2460 including duplicates. The main search was then restricted to only Nordic studies only (Table AIV-2, 163 hits) and to reviews (Table AIV-3, 444 hits).

Table AIV-1 Search terms for the main search

#	Searches	Results	Search Type
1	fishes/	134969	Advanced
2	fish/	85853	Advanced
3	fish*.ti.	91033	Advanced
4	trout/	9034	Advanced
5	trout.ti.	18286	Advanced
6	salmon/	9961	Advanced
7	salmon.ti.	12713	Advanced
8	salmo salar/	3587	Advanced
9	salmo salar.ti.	3083	Advanced
10	atlantic salmon/	3587	Advanced
11	atlantic salmon.ti.	3975	Advanced
12	seafood/	9879	Advanced
13	sea food/	9879	Advanced
14	seafood*.ti.	2038	Advanced
15	sea food.ti.	46	Advanced
16	or/1-15	219437	Advanced
17	(consumption or consumed or consuming).tw.	542993	Advanced
18	eating/	62608	Advanced
19	eating.tw.	102292	Advanced
20	intake.tw.	403880	Advanced
21	food intake/	121550	Advanced
22	dietary intake/	51974	Advanced
23	diet/	256538	Advanced
24	diet*1.tw.	529374	Advanced
25	meals/	9859	Advanced
26	meal/	9859	Advanced
27	(meal or meals).tw.	110517	Advanced
28	or/17-27	1501768	Advanced
29	16 and 28	28901	Advanced
30	(fish* adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	17161	Advanced
31	(trout adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	274	Advanced
32	(salmon* adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	540	Advanced
33	(salmo salar adj2 (eat* or intake or consum* or diet* or meal or	19	Advanced

	meals)).tw.		
34	(atlantic salmon [†] adj2 (eat [†] or intake or consum [†] or diet [†] or meal or meals)).tw.	61	Advanced
35	(seafood [†] adj2 (eat [†] or intake or consum [†] or diet [†] or meal or meals)).tw.	1598	Advanced
36	(sea-food [†] adj2 (eat [†] or intake or consum [†] or diet [†] or meal or meals)).tw.	75	Advanced
37	or/30-36	19109	Advanced
38	29 or 37	36344	Advanced
39	(mental disorder [†] adj1 (child [†] or young [†] or youth [†] or adolescen [†])).tw.	394	Advanced
40	(mental disease [†] adj1 (child [†] or young [†] or youth [†] or adolescen [†])).tw.	6	Advanced
41	(mental problem [†] adj1 (child [†] or young [†] or youth [†] or adolescen [†])).tw.	20	Advanced
42	(mental illness [†] adj1 (child [†] or young [†] or youth [†] or adolescen [†])).tw.	112	Advanced
43	allergy/	93026	Advanced
44	(allergy or allergies).tw.	135929	Advanced
45	hypersensitivity/	68448	Advanced
46	hypersensitivit [†] .tw.	107033	Advanced
47	sensitization/	29039	Advanced
48	Sensiti?ation [†] .tw.	97531	Advanced
49	immune system/	57435	Advanced
50	immune system [†] .tw.	159669	Advanced
51	immunity/	70392	Advanced
52	immunity [†] .tw.	263745	Advanced
53	autistic disorder/	47175	Advanced
54	autistic disorder [†] .tw.	2920	Advanced
55	autism/	47175	Advanced
56	autism [†] .tw.	45241	Advanced
57	birth weight/	76688	Advanced
58	birth weight [†] .tw.	94780	Advanced
59	child growth/	8920	Advanced
60	child growth [†] .tw.	1677	Advanced
61	infant growth [†] .tw.	1806	Advanced
62	child development/	71509	Advanced
63	child development [†] .tw.	9694	Advanced
64	infant development [†] .tw.	4049	Advanced
65	(child adj3 intelligence).tw.	250	Advanced
66	(child adj3 (cognition or cognitive)).tw.	923	Advanced
67	cognition/	216159	Advanced
68	cognition disorders/	142431	Advanced
69	cognitive defect/	92779	Advanced
70	(cognition [†] or cognitive [†]).tw.	490469	Advanced
71	Cognitive development/	4181	Advanced
72	Cognitive development [†] .tw.	8274	Advanced
73	intellectual impairment/	9806	Advanced

74	(Intellectual adj2 impair ⁴).tw.	3042	Advanced
75	Intellectual disability/	48976	Advanced
76	Intellectual disabilit ⁴ .tw.	15079	Advanced
77	language development/	19146	Advanced
78	language development ⁴ .tw.	6480	Advanced
79	developmental disabilities/	39965	Advanced
80	developmental disabilit ⁴ .tw.	7568	Advanced
81	developmental disorder/	25343	Advanced
82	developmental disorder ⁴ .tw.	12639	Advanced
83	neurodevelopment ⁴ .tw.	32910	Advanced
84	neuro-development ⁴ .tw.	1005	Advanced
85	infant, premature/	111252	Advanced
86	premature infant ⁴ .tw.	33494	Advanced
87	prematurity/	70662	Advanced
88	((preterm or pre-term) adj infant ⁴).tw.	35989	Advanced
89	Sexual maturation/	16260	Advanced
90	sexual maturity/	1806	Advanced
91	Sexual matur ⁴ .tw.	11304	Advanced
92	puberty/	31266	Advanced
93	pubert ⁴ .mp.	77195	Advanced
94	thyroid diseases/	35878	Advanced
95	thyroid disease/	35878	Advanced
96	thyroid disease ⁴ .tw.	22259	Advanced
97	thyroid disturbance ⁴ .tw.	141	Advanced
98	thyroid defect ⁴ .tw.	49	Advanced
99	thyroid dysfunction ⁴ .tw.	7842	Advanced
100	thyroid abnormalit ⁴ .tw.	1358	Advanced
101	Cardiovascular diseases/	277054	Advanced
102	Cardiovascular disease ⁴ .tw.	226962	Advanced
103	(cardiovascular adj event ⁴ 1).tw.	49181	Advanced
104	(cardiovascular adj death ⁴ 1).tw.	9838	Advanced
105	coronary disease/	270944	Advanced
106	coronary artery disease/	182367	Advanced
107	coronary disease ⁴ .tw.	27833	Advanced
108	coronary artery disease ⁴ .tw.	141585	Advanced
109	coronary heart disease ⁴ .tw.	90673	Advanced
110	CHD.tw.	40327	Advanced
111	cardiovascular risk/	115485	Advanced
112	cardiovascular risk ⁴ .tw.	100719	Advanced
113	cancer ⁴ .tw.	2468591	Advanced
114	neoplasms/	548916	Advanced
115	malignan ⁴ .tw.	911234	Advanced
116	Arthritis, Rheumatoid/	215294	Advanced
117	Rheumatoid Arthritis ⁴ .tw.	180352	Advanced
118	infections/	32563	Advanced
119	infection/	232020	Advanced

120	infection*.tw.	2097427	Advanced
121	risk assessment/	501193	Advanced
122	(risk adj2 assess*).tw.	116323	Advanced
123	risk factors/	1070566	Advanced
124	risk factor/	1155086	Advanced
125	risk factor*.tw.	800185	Advanced
126	risk-benefit/	39771	Advanced
127	risk-benefit*.tw.	13760	Advanced
128	benefit*.tw.	887629	Advanced
129	health hazard/	34040	Advanced
130	health hazard*.tw.	13486	Advanced
131	(health adj (effect or effects or effective or effectiveness)).tw.	36655	Advanced
132	health outcome*1.tw.	47075	Advanced
133	outcome assessment/	234863	Advanced
134	(outcome adj2 assess*).tw.	29709	Advanced
135	or/39-134	9928607	Advanced
136	38 and 135	12800	Advanced
137	limit 136 to yr="2009 -Current"	5629	Advanced
138	limit 137 to (danish or english or norwegian or swedish)	5436	Advanced
139	editorial*.pt.	797588	Advanced
140	letter*.pt.	1673999	Advanced
141	conference abstract*.pt.	1391983	Advanced
142	or/139-141	3863504	Advanced
143	138 not 142	4366	Advanced
144	animal*.mp.	1017296	Advanced
		6	
145	(rat or rats).mp.	3202148	Advanced
146	(mouse or mice).mp.	2732468	Advanced
147	or/144-146	1084335	Advanced
		7	
148	(human or humans).mp.	2907338	Advanced
		7	
149	147 not (147 and 148)	7747694	Advanced
150	143 not 149	3648	Advanced
151	remove duplicates from 150	2460	Advanced

Table AIV-2 Search terms use for Nordic studies by restriction of the main search

#	Searches	Results	Search Type
1	fishes/	134969	Advanced
2	fish/	85853	Advanced
3	fish*.ti.	91033	Advanced
4	trout/	9034	Advanced
5	trout.ti.	18286	Advanced
6	salmon/	9961	Advanced
7	salmon.ti.	12713	Advanced
8	salmo salar/	3587	Advanced
9	salmo salar.ti.	3083	Advanced
10	atlantic salmon/	3587	Advanced
11	atlantic salmon.ti.	3975	Advanced
12	seafood/	9879	Advanced
13	sea food/	9879	Advanced
14	seafood*.ti.	2038	Advanced
15	sea food.ti.	46	Advanced
16	or/1-15	219437	Advanced
17	(consumption or consumed or consuming).tw.	542993	Advanced
18	eating/	62608	Advanced
19	eating.tw.	102292	Advanced
20	intake.tw.	403880	Advanced
21	food intake/	121550	Advanced
22	dietary intake/	51974	Advanced
23	diet/	256538	Advanced
24	diet*1.tw.	529374	Advanced
25	meals/	9859	Advanced
26	meal/	9859	Advanced
27	(meal or meals).tw.	110517	Advanced
28	or/17-27	1501768	Advanced
29	16 and 28	28901	Advanced
30	(fish* adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	17161	Advanced
31	(trout adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	274	Advanced
32	(salmon* adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	540	Advanced
33	(salmo salar adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	19	Advanced

34	(atlantic salmon [†] adj2 (eat [†] or intake or consum [†] or diet [†] or meal or meals)).tw.	61	Advanced
35	(seafood [†] adj2 (eat [†] or intake or consum [†] or diet [†] or meal or meals)).tw.	1598	Advanced
36	(sea-food [†] adj2 (eat [†] or intake or consum [†] or diet [†] or meal or meals)).tw.	75	Advanced
37	or/30-36	19109	Advanced
38	29 or 37	36344	Advanced
39	(mental disorder [†] adj1 (child [†] or young [†] or youth [†] or adolescen [†])).tw.	394	Advanced
40	(mental disease [†] adj1 (child [†] or young [†] or youth [†] or adolescen [†])).tw.	6	Advanced
41	(mental problem [†] adj1 (child [†] or young [†] or youth [†] or adolescen [†])).tw.	20	Advanced
42	(mental illness [†] adj1 (child [†] or young [†] or youth [†] or adolescen [†])).tw.	112	Advanced
43	allergy/	93026	Advanced
44	(allergy or allergies).tw.	135929	Advanced
45	hypersensitivity/	68448	Advanced
46	hypersensitivit [†] .tw.	107033	Advanced
47	sensitization/	29039	Advanced
48	Sensiti?ation [†] .tw.	97531	Advanced
49	immune system/	57435	Advanced
50	immune system [†] .tw.	159669	Advanced
51	immunity/	70392	Advanced
52	immunity [†] .tw.	263745	Advanced
53	autistic disorder/	47175	Advanced
54	autistic disorder [†] .tw.	2920	Advanced
55	autism/	47175	Advanced
56	autism [†] .tw.	45241	Advanced
57	birth weight/	76688	Advanced
58	birth weight [†] .tw.	94780	Advanced
59	child growth/	8920	Advanced
60	child growth [†] .tw.	1677	Advanced
61	infant growth [†] .tw.	1806	Advanced
62	child development/	71509	Advanced
63	child development [†] .tw.	9694	Advanced
64	infant development [†] .tw.	4049	Advanced
65	(child adj3 intelligence).tw.	250	Advanced
66	(child adj3 (cognition or cognitive)).tw.	923	Advanced
67	cognition/	216159	Advanced
68	cognition disorders/	142431	Advanced
69	cognitive defect/	92779	Advanced
70	(cognition [†] or cognitive [†]).tw.	490469	Advanced
71	Cognitive development/	4181	Advanced
72	Cognitive development [†] .tw.	8274	Advanced
73	intellectual impairment/	9806	Advanced
74	(Intellectual adj2 impair [†]).tw.	3042	Advanced

75	Intellectual disability/	48976	Advanced
76	Intellectual disability [†] .tw.	15079	Advanced
77	language development/	19146	Advanced
78	language development [†] .tw.	6480	Advanced
79	developmental disabilities/	39965	Advanced
80	developmental disability [†] .tw.	7568	Advanced
81	developmental disorder/	25343	Advanced
82	developmental disorder [†] .tw.	12639	Advanced
83	neurodevelopment [†] .tw.	32910	Advanced
84	neuro-development [†] .tw.	1005	Advanced
85	infant, premature/	111252	Advanced
86	premature infant [†] .tw.	33494	Advanced
87	prematurity/	70662	Advanced
88	((preterm or pre-term) adj infant [†]).tw.	35989	Advanced
89	Sexual maturation/	16260	Advanced
90	sexual maturity/	1806	Advanced
91	Sexual matur [†] .tw.	11304	Advanced
92	puberty/	31266	Advanced
93	pubert [†] .mp.	77195	Advanced
94	thyroid diseases/	35878	Advanced
95	thyroid disease/	35878	Advanced
96	thyroid disease [†] .tw.	22259	Advanced
97	thyroid disturbance [†] .tw.	141	Advanced
98	thyroid defect [†] .tw.	49	Advanced
99	thyroid dysfunction [†] .tw.	7842	Advanced
100	thyroid abnormalit [†] .tw.	1358	Advanced
101	Cardiovascular diseases/	277054	Advanced
102	Cardiovascular disease [†] .tw.	226962	Advanced
103	(cardiovascular adj event [†] 1).tw.	49181	Advanced
104	(cardiovascular adj death [†] 1).tw.	9838	Advanced
105	coronary disease/	270944	Advanced
106	coronary artery disease/	182367	Advanced
107	coronary disease [†] .tw.	27833	Advanced
108	coronary artery disease [†] .tw.	141585	Advanced
109	coronary heart disease [†] .tw.	90673	Advanced
110	CHD.tw.	40327	Advanced
111	cardiovascular risk/	115485	Advanced
112	cardiovascular risk [†] .tw.	100719	Advanced
113	cancer [†] .tw.	2468591	Advanced
114	neoplasms/	548916	Advanced
115	malignan [†] .tw.	911234	Advanced
116	Arthritis, Rheumatoid/	215294	Advanced
117	Rheumatoid Arthritis [†] .tw.	180352	Advanced
118	infections/	32563	Advanced
119	infection/	232020	Advanced
120	infection [†] .tw.	2097427	Advanced

121	risk assessment/	501193	Advanced
122	(risk adj2 assess*).tw.	116323	Advanced
123	risk factors/	1070566	Advanced
124	risk factor/	1155086	Advanced
125	risk factor*.tw.	800185	Advanced
126	risk-benefit/	39771	Advanced
127	risk-benefit*.tw.	13760	Advanced
128	benefit*.tw.	887629	Advanced
129	health hazard/	34040	Advanced
130	health hazard*.tw.	13486	Advanced
131	(health adj (effect or effects or effective or effectiveness)).tw.	36655	Advanced
132	health outcome*1.tw.	47075	Advanced
133	outcome assessment/	234863	Advanced
134	(outcome adj2 assess*).tw.	29709	Advanced
135	or/39-134	9928607	Advanced
136	38 and 135	12800	Advanced
137	limit 136 to yr="2009 -Current"	5629	Advanced
138	limit 137 to (danish or english or norwegian or swedish)	5436	Advanced
139	editorial*.pt.	797588	Advanced
140	letter*.pt.	1673999	Advanced
141	conference abstract*.pt.	1391983	Advanced
142	or/139-141	3863504	Advanced
143	138 not 142	4366	Advanced
144	animal*.mp.	10172966	Advanced
145	(rat or rats).mp.	3202148	Advanced
146	(mouse or mice).mp.	2732468	Advanced
147	or/144-146	10843357	Advanced
148	(human or humans).mp.	29073387	Advanced
149	147 not (147 and 148)	7747694	Advanced
150	143 not 149	3648	Advanced
151	remove duplicates from 150	2460	Advanced
152	norway/	60246	Advanced
153	(norway* or norwegian*).tw.	66628	Advanced
154	sweden/	114504	Advanced
155	(sweden* or swedish*).tw.	115032	Advanced
156	denmark/	73342	Advanced
157	(denmark* or danish*).tw.	74581	Advanced
158	iceland/	7279	Advanced
159	iceland*.tw.	9009	Advanced
160	finland/	55192	Advanced
161	(finland* or finnish*).tw.	59796	Advanced
162	or/152-161	436439	Advanced
163	151 and 162	163	Advanced

Table AIV-3 Search terms use for review by restriction of the main search

#	Searches	Results	Search Type
1	fishes/	134969	Advanced
2	fish/	85853	Advanced
3	fish*.ti.	91033	Advanced
4	trout/	9034	Advanced
5	trout.ti.	18286	Advanced
6	salmon/	9961	Advanced
7	salmon.ti.	12713	Advanced
8	salmo salar/	3587	Advanced
9	salmo salar.ti.	3083	Advanced
10	atlantic salmon/	3587	Advanced
11	atlantic salmon.ti.	3975	Advanced
12	seafood/	9879	Advanced
13	sea food/	9879	Advanced
14	seafood*.ti.	2038	Advanced
15	sea food.ti.	46	Advanced
16	or/1-15	219437	Advanced
17	(consumption or consumed or consuming).tw.	542993	Advanced
18	eating/	62608	Advanced
19	eating.tw.	102292	Advanced
20	intake.tw.	403880	Advanced
21	food intake/	121550	Advanced
22	dietary intake/	51974	Advanced
23	diet/	256538	Advanced
24	diet*1.tw.	529374	Advanced
25	meals/	9859	Advanced
26	meal/	9859	Advanced
27	(meal or meals).tw.	110517	Advanced
28	or/17-27	1501768	Advanced
29	16 and 28	28901	Advanced
30	(fish* adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	17161	Advanced
31	(trout adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	274	Advanced
32	(salmon* adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	540	Advanced
33	(salmo salar adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	19	Advanced

34	(atlantic salmon* adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	61	Advanced
35	(seafood* adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	1598	Advanced
36	(sea-food* adj2 (eat* or intake or consum* or diet* or meal or meals)).tw.	75	Advanced
37	or/30-36	19109	Advanced
38	29 or 37	36344	Advanced
39	(mental disorder* adj1 (child* or young* or youth* or adolescen*)).tw.	394	Advanced
40	(mental disease* adj1 (child* or young* or youth* or adolescen*)).tw.	6	Advanced
41	(mental problem* adj1 (child* or young* or youth* or adolescen*)).tw.	20	Advanced
42	(mental illness* adj1 (child* or young* or youth* or adolescen*)).tw.	112	Advanced
43	allergy/	93026	Advanced
44	(allergy or allergies).tw.	135929	Advanced
45	hypersensitivity/	68448	Advanced
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53	autistic disorder/	47175	Advanced
54	autistic disorder*.tw.	2920	Advanced
55	autism/	47175	Advanced
56	autism*.tw.	45241	Advanced
57	birth weight/	76688	Advanced
58	birth weight*.tw.	94780	Advanced
59	child growth/	8920	Advanced
60	child growth*.tw.	1677	Advanced
61	infant growth*.tw.	1806	Advanced
62	child development/	71509	Advanced
63	child development*.tw.	9694	Advanced
64	infant development*.tw.	4049	Advanced
65	(child adj3 intelligence).tw.	250	Advanced
66	(child adj3 (cognition or cognitive)).tw.	923	Advanced
67	cognition/	216159	Advanced
68	cognition disorders/	142431	Advanced
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70	(cognition* or cognitive*).tw.	490469	Advanced
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79	developmental disabilities/	39965	Advanced
80	developmental disability [†] .tw.	7568	Advanced
81	developmental disorder/	25343	Advanced
82	developmental disorder [†] .tw.	12639	Advanced
83	neurodevelopment [†] .tw.	32910	Advanced
84	neuro-development [†] .tw.	1005	Advanced
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87	prematurity/	70662	Advanced
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96	thyroid disease [†] .tw.	22259	Advanced
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108	coronary artery disease [†] .tw.	141585	Advanced
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114	neoplasms/	548916	Advanced
115	malignan [†] .tw.	911234	Advanced
116	Arthritis, Rheumatoid/	215294	Advanced
117	Rheumatoid Arthritis [†] .tw.	180352	Advanced
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124	risk factor/	1155086	Advanced
125	risk factor*.tw.	800185	Advanced
126	risk-benefit/	39771	Advanced
127	risk-benefit*.tw.	13760	Advanced
128	benefit*.tw.	887629	Advanced
129	health hazard/	34040	Advanced
130	health hazard*.tw.	13486	Advanced
131	(health adj (effect or effects or effective or effectiveness)).tw.	36655	Advanced
132	health outcome*1.tw.	47075	Advanced
133	outcome assessment/	234863	Advanced
134	(outcome adj2 assess*).tw.	29709	Advanced
135	or/39-134	9928607	Advanced
136	38 and 135	12800	Advanced
137	limit 136 to yr="2009 -Current"	5629	Advanced
138	limit 137 to (danish or english or norwegian or swedish)	5436	Advanced
139	editorial*.pt.	797588	Advanced
140	letter*.pt.	1673999	Advanced
141	conference abstract*.pt.	1391983	Advanced
142	or/139-141	3863504	Advanced
143	138 not 142	4366	Advanced
144	animal*.mp.	10172966	Advanced
145	(rat or rats).mp.	3202148	Advanced
146	(mouse or mice).mp.	2732468	Advanced
147	or/144-146	10843357	Advanced
148	(human or humans).mp.	29073387	Advanced
149	147 not (147 and 148)	7747694	Advanced
150	143 not 149	3648	Advanced
151	remove duplicates from 150	2460	Advanced
152	(systematic adj (review*1 or overview*1)).mp.	154877	Advanced
153	(literature adj1 review*1).tw.	99776	Advanced
154	review.pt.	3801982	Advanced
155	(meta analy* or metaanaly*).mp.	201805	Advanced
156	cochrane.tw.	66989	Advanced
157	or/152-156	4013230	Advanced
158	151 and 157	444	Advanced

Appendix V

Search terms for supplementary n-3 fatty acids (EPA and/or DHA) and health outcomes

In the main text Chapter 4 addresses “Health effects associated with fish consumption – epidemiological studies”. Thus, the main literature search (Appendix IV) aimed to retrieve studies addressing fish consumption and health outcomes. However, in addition a secondary search was conducted aiming to identify whether new scientific evidence would imply a change in the previously established beneficial effects of supplementary EPA and/or DHA in prevention of cardiovascular diseases. The same search strategy as in the VKM report of 2011 which evaluated negative and positive health effects of n-3 fatty acids as constituents of food supplements and fortified foods was used, but the search period was limited from 2009. The search was performed 16. December 2013 and the search terms used were as follows:

MEDLINE

VKM_Fish_Oils_3_MEDLINE

Metaanalyser, systematic reviews:

1. Eicosapentaenoic Acid/
2. eicosapentaenoic acid*.mp.
3. Docosahexaenoic Acids/
4. Docosahexaenoic Acid*.mp.
5. Fatty Acids, Omega-3/
6. omega-3 fatty acid*.mp.
7. Fish Oils/
8. fish oil*.mp.
9. fish liver oil*.mp.
10. Cod Liver Oil/
11. cod liver oil*.mp.
12. cod oil*.mp.
13. alpha-Linolenic Acid/
14. alpha linolenic acid*.mp.
15. or/1-14
16. ae.xs.
17. adverse effect*.mp.
18. adverse event*.mp.
19. Risk Assessment/
20. risk factor*.mp.
21. Toxicity Tests/
22. toxicity.mp.
23. toxic.mp.

24. Dose-Response Relationship, Drug/
25. Dose-Response.mp.
26. or/16-25
27. 15 and 26
28. Oxidative Stress/
29. oxidative stress.mp.
30. stress oxidative.mp.
31. Lipid Peroxides/
32. Lipid Peroxidation/
33. lipid peroxid*.mp.
34. Peroxides/
35. peroxides.mp.
36. Malondialdehyde/
37. malondialdehyde.mp.
38. Thiobarbiturates/
39. Thiobarbiturate*.mp.
40. Thiobarbituric Acid Reactive Substances/
41. Thiobarbituric Acid*.mp.
42. or/28-41
43. 15 and 27
44. 15 and 42
45. or/43-44
46. Meta-Analysis/
47. Meta-Analysis as Topic/
48. meta analy*.mp.
49. metaanaly*.mp.
50. (systematic adj (review*1 or overview*1)).mp.
51. exp "Review Literature as Topic"/
52. or/46-51
53. 45 and 52
54. limit 53 to yr="2000 -Current"

EMBASE

VKM_Fish_Oils_3_EMBASE

Metaanalyser, systematisc reviews:

1. eicosapentaenoic acid/
2. eicosapentaenoic acid*.mp.
3. docosahexaenoic acid/
4. docosahexaenoic acid*.mp.
5. omega 3 fatty acid/
6. omega 3 fatty acid*.mp.
7. fish oil/
8. fish oil*.mp.

9. fish liver oil*.mp.
10. cod liver oil/
11. cod liver oil*.mp.
12. cod oil*.mp.
13. linolenic acid/
14. alpha-linolenic acid*.mp.
15. or/1-14
16. adverse effect*.mp.
17. adverse event*.mp.
18. risk assessment/
19. risk assessment.mp.
20. risk factor*.mp.
21. toxicity testing/
22. toxicity.mp.
23. toxic.mp.
24. dose response/
25. dose response.mp.
26. or/16-24
27. oxidative stress/
28. oxidative stress.mp.
29. stress oxidative.mp.
30. lipid peroxide/
31. lipid peroxidation/
32. lipid peroxid*.mp.
33. peroxide/
34. peroxide*.mp.
35. malonaldehyde/
36. malonaldehyde.mp.
37. malondialdehyde.mp.
38. thiobarbituric acid/
39. thiobarbituric acid*.mp.
40. thiobarbiturate*.mp.
41. or/27-40
42. 15 and 26
43. 15 and 41
44. or/42-43
45. meta analysis/
46. meta analy*.mp.
47. metaanaly*.mp.
48. (systematic adj (review*1 or overview*1)).mp.
49. or/45-48
50. 44 and 49
51. conference abstract.pt.
52. letter.pt.

53. editorial*.pt.
54. or/51-53
55. 50 not 54
56. limit 55 to yr="2000 -Current"
57. (animal* not (animal* and human*)).mp.
58. 56 not 57
59. limit 58 to (danish or english or norwegian or swedish)

Appendix VI

Description of sampling, methods for chemical analyses and quality assurance of nutrients and contaminants in fish

This appendix provides detailed information about the background for the tables in Chapter 6 Nutrients and contaminants in fish on the Norwegian market.

The content of this appendix is as follows:

AVI-1 Description of collection of farmed and wild fish for analyses of nutrients and contaminants

- Farmed Atlantic salmon and trout – sampling for analyses of contaminants
- Base line studies – sampling for analyses of contaminants
 - Herring – Norwegian spring spawning (NVG herring). Data used for calculating exposure and nutrient intake in the current report
 - Herring – North Sea. Data not used to calculate exposure or nutrient intake in the current report
 - Mackerel
 - Atlantic cod
 - Saithe
 - Greenland halibut
- Atlantic halibut – sampling for analyses of contaminants
- Wild Atlantic salmon – sampling for analyses of contaminants
- Samples of other species, fish oils and canned fish for analyses contaminants
- Sampling of farmed and wild fish for analyses of nutrients

AVI-2 Methods for chemical analyses and quality assurance of nutrients and contaminants in fish

- Nutrients
- Contaminants: Description of the limit of detection (LOD) and the limit of quantification (LOQ) for dioxins and dioxin-like PCBs (dl-PCBs)

AVI-1 Description of collection of farmed and wild fish for analyses of nutrients and contaminants

• Farmed Atlantic salmon and trout – sampling for analyses of contaminants

The samples of farmed Atlantic salmon and trout analysed and data used for this report is based on market-size fish (3-5 kg) sampled at processing plants (Hannisdal et al., 2014) as part of the annual surveillance project of farmed fish. In this program, residues of therapeutic agents, illegal substances, and other substances in Norwegian farmed fish are measured in accordance with the Directive 96/23/EC "On measures to monitor certain substances and residues thereof in live animal and animal products". The Norwegian Food Safety Authority (NFSA) is responsible for the enforcement, planning, and sampling, following up this directive in Norway, while NIFES is responsible for the analysis. The scope of sampling is based on total production (minimum 1 sample per 100 tonnes produced), and is randomised with regards to season and region in the whole of coastal Norway, and the sample identification is blinded for the analysts. Samples of fish muscle were transported to NIFES in a frozen state. On arrival at NIFES, the Norwegian quality cut (NQC) was obtained from the fish (Johnsen et al., 2011). Pooled sample of five fish from the same cage/farm were homogenised before analyses.

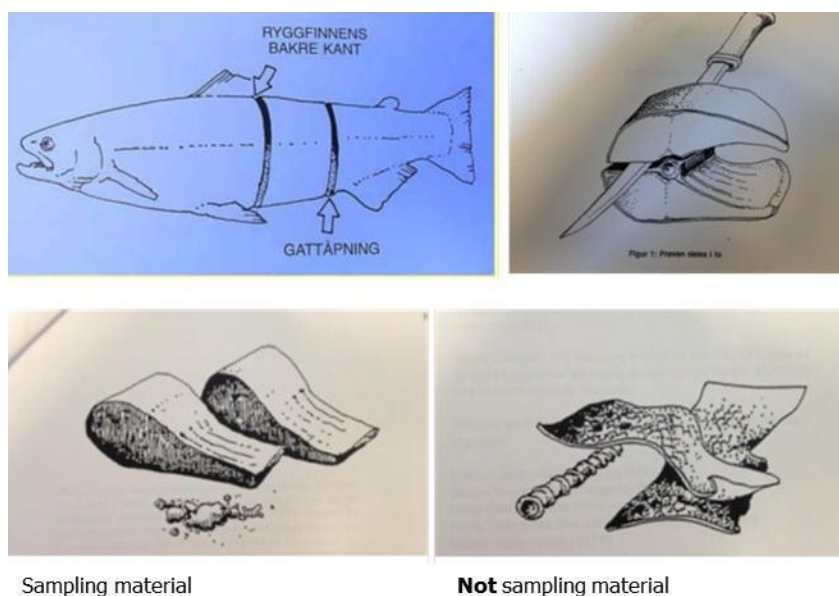


Figure AVI-1 Illustration of Norwegian Quality Cut (NQC) for Atlantic salmon and Rainbow trout. Upper left picture show the area which is sampled between the posterior part of the back fin and anterior part of the gut. Upper right picture show how the sample is divided into two fillet parts. Lower left picture show the part of the fillet that is included in the NQC sample for further chemical analyses. Lower right picture show the material that is not included in the NQC sample. Source: Norwegian standard 1994.

- **Base line studies – sampling for analyses of contaminants**

The majority of wild fish species analysed for contaminants and used for calculations in this report are from comprehensive baseline studies performed by NIFES. The general goal of the baseline studies is to reflect commercial fisheries in Norwegian waters, while also trying to cover the widest possible part of the distribution area of the species as well as all seasons and the relevant size range of the fish. The number of samples from different areas was selected in collaboration with researchers from the Institute of Marine Research based on fisheries statistics and geographic distribution area of the species. Fish were caught mainly using the reference fleet, which are commercial fishing vessels assisting IMR with sampling of fish either as part of their commercial fishing or as special assignments. These are the same vessels which are used for IMR fish population estimates. If nothing else is stated, determinations of Hg, dioxins and PCBs were performed on fish fillets without skin but with the sub-cutaneous fat scraped off the skin and included in the sample.

- **Herring – Norwegian Spring Spawning (NVG herring). Data used for calculating exposure and nutrient intake in the current report**

Norwegian spring spawning herring (NSS herring) migrate in large schools in different areas at different times of the year.

Samples of NSS herring were taken during the spawning season from January to February along the Norwegian coast (63-68°N, 200 fish) and after spawning in April-June (225 fish) and in August-October (375 fish) in the Norwegian Sea (65-73°N, from outside the Norwegian coast and as far west as Iceland). No samples were collected during wintering in West Fjord or off the coast of northern Norway.

Data for age, size, gender and fat contents from the final report are shown in Table AV-1 below. Fish of all sizes were sampled from the catches.

Fish age and size were very important factors for concentrations of both Hg and organic pollutants in NSS herring, where concentrations increased with increasing size and age. For organic pollutants the time of year was of great significance since the highest concentrations were measured in herring from January-February, before spawning, and the lowest in spring, after spawning. January-February and October are important commercial fishing seasons for NSS herring, while in March-April much less is being caught. Hence, not all the samples in the project are equally representative of the commercially available herring for consumption.

Table AV-1 Information about the 800 sampled and analysed NVG herring

NVG herring	n	Mean	Std	Minimum	Maximum
Weight (g)	800	276	89	76	536
Length (cm)	800	31.4	2.6	23	38
Age (years)	727	6.2	2.5	3	16
Sex (%)	660	50.5 ♂ + 49.5 ♀	No data	No data	No data
Lipid content (g/100g)	800	11.8	6.3	1.3	27

Source: All data are described and reported by Frantzen et al. (2009)

- **Herring – North Sea. Data not used to calculate exposure or nutrient intake in the current report.**

The samples for the baseline study were mainly derived from commercial catches. The size of the fish varied widely from catch to catch, but they were all appropriate for different markets. The samples were collected to cover the entire area of distribution of North Sea herring for all seasons, and for instance some of the samples were taken around the English Channel in December and February. These samples were particularly high in dioxins and are not representative of the commercially available North Sea herring. These are part of what we have defined as the southern component (we have provided data both on all samples from the open sea and separated into a northern and a southern component). In the northern part two samples were included which were caught as by-catch in the mackerel fishery, with particular old and shed herring particularly high in cadmium. These are also probably less relevant for the market. Hence, North Sea herring data were not used for exposure and nutrient intake calculations. North Sea herring data are, however, included in the tables to show the variation in herring nutrient and contaminant concentrations.

All data are described and reported by Duinker et al. (2013).

- **Mackerel**

Sample material was selected in collaboration with the Institute of Marine Research based on catch statistics and the geographic distribution of the species at the time the baseline study was conducted. Since then, the mackerel migration patterns changed and mackerel is now being fished to a greater extent in the Norwegian Sea.

Most samples were collected in autumn, during the period from August to November. Samples from three positions were collected in the spring, in March, April and June. Most samples were collected in the North Sea, particularly during the period from October to November. In September, samples were also taken from two locations in the Skagerrak and four positions in the Norwegian Sea off northern Norway. The samples collected in March and April, were taken west of Scotland. Analyses were performed on fish fillets without skin. For overview, see Table AVI-2.

Table AVI-2 Information about the analysed mackerel

Mackerel	Samples type	n	Mean	Std	Minimum	Maximum
Age (years)	All fish	1170	4.3	2.5	0	15
	Fish analysed for metals	831 ^a	4.1	2.6	0	15
	Fish analysed for POPs	803 ^a	4.6	2.5	1	15
Lenght (cm)	All fish	1191	33.4	4.6	18	44
	Fish analysed for metals	845	32.7	4.9	19	43
	Fish analysed for POPs	818	33.8	4.5	20	44
Weight (g)	All fish	1191	352	146	35	774
	Fish analysed for metals	845	325	146	49	773
	Fish analysed for POPs	818	367	141	51	774

Mackerel	Samples type	n	Mean	Std	Minimum	Maximum
Fillet lipid (g/100g)	All fish	1166	21.5	8.9	1.2	41
	Fish analysed for metals	845	19.2	8.8	1.2	39
	Fish analysed for POPs	818	22.0	9.3	1.2	41
Sex (%)	All fish	787	51.2	-	-	-
	Fish analysed for metals	468	50.0	-	-	-
	Fish analysed for POPs	764	51.3	-	-	-

^aNot possible to decide age for all the fish

Source: All data are described and reported by Frantzen et al. (2010)

o **Atlantic cod**

Samples of Atlantic cod were collected at 84 positions in the species' entire Norwegian distribution area from the north east Barents Sea in the north to the North Sea in the south, based on catch statistics. The samples included both 804 ocean caught cod from 33 positions in the Barents Sea (Northeast arctic cod), 585 ocean caught cod from 24 positions in the North Sea (North Sea cod) and 675 coastal and fjord cod from 27 different positions mainly in the fjords. The data in this report is divided into three cod stocks to differentiate between the three populations; Northeast arctic cod, which has the lowest concentrations of contaminants and is the most representative with respect to consumption, North Sea cod which has intermediate concentrations, and the coastal and fjord cod which has the highest levels of contaminants. To calculate contaminant exposure and nutrient intake, mean concentrations of the three populations were used.

Although Atlantic cod were collected from all quarters of the year the numbers of fish caught during the different seasons reflect the main fishing seasons for each fishing area.

For overview, see Table AVI-3.

Table AVI-3 Information about the analysed Atlantic cod sampled from three different sea areas. Data are given as mean±std with minimum and maximum values given in brackets.

Samples	North-East arctic	Coast/fjord	North Sea
Number of fish	804	675	585
Age (year)	5.9±1.5 (3-13)	5.2±2.0 (2-12)	3.9±1.3 (2-8)
Length (cm)	65±13 (37-110)	60±12 (33-103)	63±16 (29-100)
Weight (kg)	2.5±1.6 (0.5-14.3)	2.7±1.7 (0.3-14.2)	3.2±2.5 (0.3-11.2)
Liver weight (g)	102±93 (8-630)	105±135 (2-1106)	149±178 (1-1095)
Dry matter (g/100g)	192±35 (178-228)	191±12 (134-222)	194±95 (164-235)
Liver lipids (g/100g)	51±13 (6-84)	47±15 (8-84)	51±13 (5-71)

Source: All data are described and reported by Julshamn et al. (2013a); Julshamn et al. (2013b); Julshamn et al. (2013c); Julshamn et al. (2013d).

- **Saithe**

Two baseline studies for saithe have been performed, one for Northeast Arctic saithe from the Norwegian Sea and the Barents Sea and another for saithe in the North Sea. The data used in this report are all data combined representing the range of commercially available saithe.

In the two baseline studies saithe were sampled from a total of 41 positions from the entire area of distribution from the northeast Barents Sea in the North to the North Sea in the south. The samples included 485 fish from 15 positions in the Barents Sea (Northeast Arctic saithe), 471 fish from 19 positions in the Norwegian Sea (Northeast Arctic saithe) and 664 fish from 27 positions in the North Sea (North Sea saithe). In all the regions fish were gathered from both coastal and fjord areas and from the open sea. Commercially, Northeast Arctic saithe are more important than saithe from the North Sea. To reflect this, more fish were collected from the Norwegian Sea and the Barents Sea than from the North Sea.

The concentration of mercury in the fillet and organic contaminants in the liver of saithe were highest in saithe from the North Sea and lowest in saithe from the Barents Sea. However, concentrations also increased with increasing fish age and size.

For overview, see Table AVI-4.

Table AVI-4 Information about the analysed saithe sampled from two different sea areas. Data are given as mean±std with minimum and maximum values given in brackets.

Parameters	Saithe, Northeast arctic		Saithe, North sea		Saithe, all	
	n	mean ± std (min-max)	n	mean ± std (min-max)	n	mean ± std (min-max)
Age (years)	856	5.4 ± 2.2 (2-18)	663	5.2 ± 1.6 (2-12)	1519	5.3 ± 1.9 (2-18)
Lenght (cm)	956	52 ± 12 (33-100)	664	49 ± 9 (35-82)	1620	51 ± 11 (33-100)
Weight (g)	956	1.8 ±1.3 (0.50-9.0)	664	1.5 ± 1.0 (0.32-5.1)	1620	1.7 ±1.2 (0.32-9.0)
Liver weight	902	116 ± 113 (8.8-1000)	639	79 ± 96 (4.7 -505)	1541	100 ± 108 (4.7-1000)
Liver lipid (g/100g)	951	60 ± 11 (4.1-86)	580	50 ± 18 (4.8-87)	1552	56 ± 15 (3.7-87)

Source: All data are described and reported by Nilsen et al. (2013a); Nilsen et al. (2012).

- **Greenland halibut**

Samples were collected of Greenland halibut from a total of 27 positions from the entire area of distribution along the Norwegian continental shelf edge from about 63°N to 77°N (west of Svalbard) and in the Barents Sea off the coast of eastern Finnmark. Most samples were collected in an area from Lofoten to Tromsøflaket (454 fish from 10 positions) which is the main area for commercial fishing of Greenland halibut. In addition, 342 fish from seven

locations in the area south of Lofoten, 300 fish from six positions in the area west of Bear Island and Svalbard and 192 fish from four locations off the coast of eastern Finnmark, were collected. For overview, see Table AVI-5.

The amount of samples in different quarters of the year reflected the Greenland halibut commercial fishery. Samples were collected during the first, second and third quarter of the year, but not during the fourth quarter since hardly any Greenland halibut fishing is done during this period.

The most pronounced variations in the concentration of mercury and persistent organic pollutants in Greenland halibut were due to geographical area with concentrations of mercury and persistent organic pollutants being lowest in fish caught off eastern Finnmark. The highest levels of POPs were found in Greenland halibut from the area south of Lofoten, and consequently, some of these fishing areas were closed for commercial fishing by the Norwegian Directorate of fisheries due to increased risk of exceeding upper limits for contaminants. Data on contaminant levels from this area from the follow up of base line studies after 2010 have not been included in this report (but are available at www.nifes.no/sjomatdata), as these are not representative for commercially available Greenland halibut.

The concentration of mercury increased with increasing fish age and size and decreased with increasing fat content of the fillet. There was, however, no correlation found between the concentration of organic contaminants and Greenland halibut age, size or fat content.

Table AVI-5 Information about the analysed Greenland halibut

Parameter	n	Mean	Std	Minimum	Maximum
Length (cm)	1288	66	7	41	90
Weight (g)	1288	3075	1146	665	8795
Fillet lipids (g/100 g)	1288	11	3.3	1.1	23
Age (years)	716	17.8	3.1	7	28
Sex distribution (%)	1288	12 ♂+ 88 ♀	No data	No data	No data

Source: All data are described and reported by Nilsen et al. (2010).

- **Atlantic halibut – sampling for analyses of contaminants**

The samples of Atlantic halibut reported here are not from a complete baseline study, but collected from separate smaller surveys from 2006 to 2010, where a total of 90 fish were analysed. In the different studies, different parts of the fish fillet were sampled and analysed, but the majority of the fish were analysed as B-section and I-section and then combining the two to give a mean content of Hg and POPs (Figure AV-2). The I-section contains more fat and hence more POPs, whereas the B-section is leaner with less POPs. The halibut collected in 2006 were not divided into I-section and B-section, but analysed as whole fillets. The 20 halibut from 2007 were caught in the Norwegian Sea in September 2007, and had a weight range from 47.6 to 80 kg. The second study included 22 halibut

caught in the period from February 2008 to May 2010, all caught north of 69°N. Here, fish weight ranged from 1.7 to 70.5 kg (Table AVI-6). Since fat contents and contaminant concentrations increase with increasing halibut size (Figure AVI-3) it is important to have a range of sizes represented in the data material, as is the case in the data used for this report with halibut weight ranging from 1.7 kg to 70.5 kg.

Table AVI-6 Sampling position, length (cm) and weight (kg) of individual Atlantic halibut sampled in North Norway during 2008-2010

Sampling site	Sampling date	Length (cm)	Weight (kg)
70°25'N 19°28'E	22.02.08	58	1.7
70°25'N 19°28'E	22.02.08	63	2.0
70°41'N 21°43'E	20.02.08	67	2.6
Hammerfest havn	01.05.09	64	3.2
69°24'N 15°52'E	27.02.08	70	3.4
70°45'N 28°08'E	24.04.08	74	3.6
69°24'N 15°52'E	27.02.08	76	4.3
70°59'N 23°29'E	06.05.10	78	5.3
70°59'N 23°29'E	06.05.09	90	7.2
70°40'N 23°41'E	06.06.09	88	8.0
71°05'N 27°17'E	25.08.08	93	8.1
71°05'N 27°17'E	25.08.08	91	8.3
69°52'N 15°57'E	04.09.08	117	18.3
70°00'N 18°15'E	07.04.08	123	19.5
72°07'N 17°40'E	21.01.09	144	41.5
Vesterålen	04.09.08	Unknown	45.0
Troms	20.09.08	Unknown	53.5
Nordland	19.09.08	Unknown	53.7
Vesterålen/Troms	09.08.08	Unknown	60.3
Vesterålen	04.09.08	Unknown	70.5

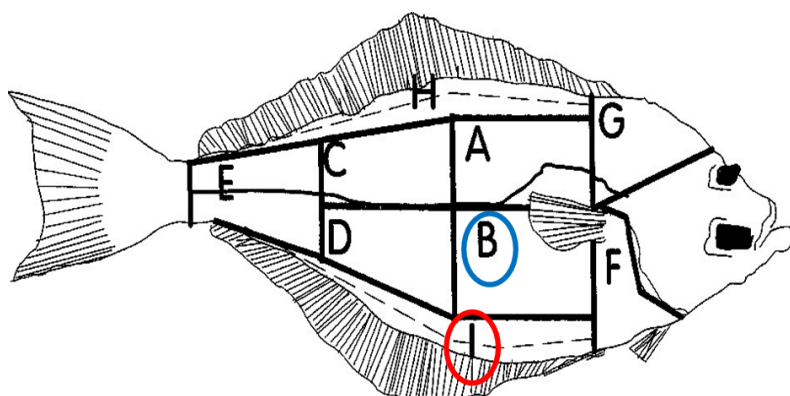


Figure AVI-2 Different cuts from Atlantic halibut. The two cuts referred to in the description of sampling are highlighted by a blue circle (B-cut) and red circle (I-cut, which runs along one of the fins of the halibut). Source: Nortvedt and Tuene (1998)

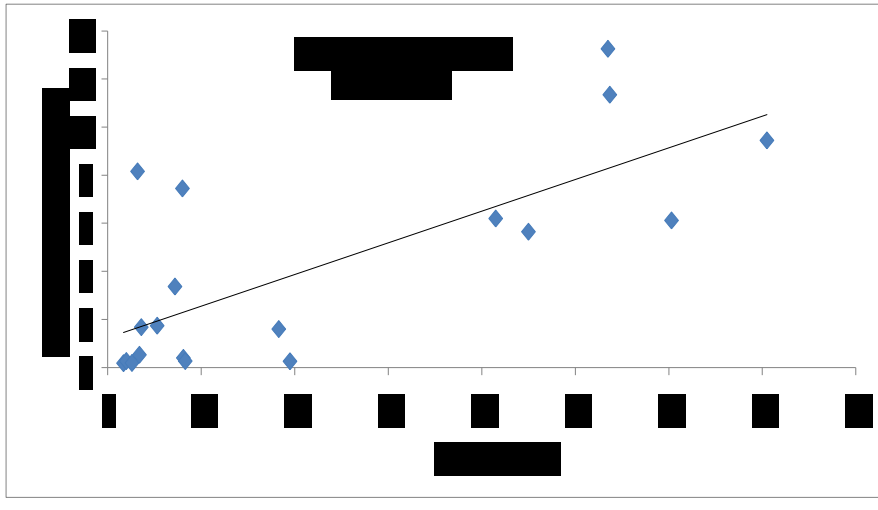


Figure AVI-3 Weight (kg) of Atlantic halibut (I-cut) at the x-axis and dioxins and dl-PCBs (ng TEQ/kg ww) in fillet at the y-axis. Increased halibut size is followed by increased content of body fat and increased concentration of dioxins and dioxin-like PCBs. Source: Julshamn et al. (2007); Julshamn et al. (2011)

- **Wild Atlantic salmon – sampling for analyses of contaminants**

The sample materials were provided by a project led by the Institute of Marine Research. Wild Atlantic salmon were caught by local fishermen in six areas in northern Norway based on the known local geographic distribution range of the species. Between 22 and 167 fish were collected per site (total 422 wild salmon), and the average fish length and weight ranged from 62 to 77 cm and from 2.5 to 5.1 kg. There were significant differences in the size of individual fish and the weight ranged from 1.1 to 18.4 kg. The data used in this report are analysis 20 Atlantic salmon fillets from five different localities (only 18 fish from one locality). Wild Atlantic salmon of comparable size as farmed Atlantic salmon of approximately 2.5-5 kg were selected for analyses. Data are described by Lundebye et al. (manuscript in prep.; pers. comm.).

- **Samples of other species, fish oils and canned fish for analyses contaminants**

Samples of commercially relevant size of different fish being relevant for small scale commercial fisheries and consumption was sampled by NIFES in surveillance programs and analysed for selected contaminants. In this report, data is on consumption size relevant redfish (n=13), wolffish (n=10), plaice (n=25), haddock (n=7) and sprat (n=14) (www.nifes.no/sjomatdata). A selection of canned tuna (n=6) and cod roe and liver pate (Svolværpostei, one pooled sample based on five cans) and various fish oils for human consumption sampled over the years from 2006 to 2013 was analysed by NIFES.

Data for contaminants are described and reported in annual reports to the NFSA, «Miljøgifter i fisk og fiskevarer», available at www.nifes.no and www.mattilsynet.no.

- **Sampling of farmed and wild fish for analyses of nutrients**

Nutrients analyses were performed on a selected and limited number of fish from the annual surveillance program of farmed Atlantic salmon (Hannisdal et al., 2014), and from the baseline studies for NVG herring, north sea herring, Greenland halibut, Atlantic cod, saithe and mackerel described above. If nothing else is stated, analyses were performed on fillets without skin of fish selected to be relevant size for consumption (www.nifes.no/sjomatdata). Nutrients of wild Atlantic salmon were analysed in fish sampled by two IMR projects, one of wild Atlantic salmon in Sør fjorden ("Vossolaks"; n=27) and another of wild Atlantic salmon off the Finnmark coast as described above (Lundebye et al., manuscript in prep.; pers. comm.; n=97).

Atlantic halibut collected for nutrient analyses were sampled from two ocean areas (Norskehavet and Nordsjøen) and are not from the same sample batches described above for contaminant analyses. For these fish, only the leaner part of the fillet (A and B cuts, see Figure AV-1) were sampled and analysed, explaining the relative low lipid content (2.3%) compared to what reported in "Matvaretabellen" (6.1%). The fish size varied from 0.5 kg to 40kg, which cover relevant consumer sized halibut.

Wolffish and plaice of relevant consumer sizes were sampled random from commercial fishing sites but not as part of a larger base line study and analysed by NIFES.

Fish oils analysed for nutrients were a selection of oils from the material described above as part of the annual surveillance project by NIFES for the NFSA «Miljøgifter i fisk og fiskevarer» available at www.nifes.no and www.mattilsynet.no.

AVI-2 Methods for chemical analyses and quality assurance of nutrients and contaminants in fish

The NIFES laboratory routines and data reported in this chapter are based on analytical methods which are accredited in accordance with the standard ISO 17025. The analytical methods for the contaminants and their Limit of detection (LOD) and Limit of quantification (LOQ) are described for each set of data in all reports where the data were reported by Duinker et al. (2013); Frantzen et al. (2009); Frantzen et al. (2010); Hannisdal et al. (2014); Julshamn et al. (2010); Julshamn et al. (2007); Julshamn et al. (2013d); Nilsen et al. (2013a); Nilsen et al. (2010); Nilsen et al. (2012). The limit of detection (LOD) is the lowest level at which the method is able to detect the substance, while the limit of quantification (LOQ) is the lowest level for a reliable (Duinker et al., 2013) quantitative measurement. For all methods, a quality control sample (QCS) with a known composition and concentration of target analyte, is included in each series. The QCS results are checked to be within pre-defined limits before the results are approved. The methods are regularly verified by participation in inter laboratory proficiency tests, or by analysing certified reference material (CRM), where such exist. Since analytical methodology is constantly improving, sensitivity and accuracy may increase resulting in decreased LOQ and LOD over time for quantification of contaminants and nutrients.

- **Nutrients**

For chemical analyses of nutrient, the methodological principle and limits of quantifications (LOQs) are given in Table AVI-7.

Table AVI-7 Method principle, limit of quantification for the main methodology used for analyses of farmed and wild fish species and fish oils. All methods are accredited according to ISO standards.

Parameter	Method principle	Limit of quantification (LOQ)
Total lipids	Ethyl acetate	0.1 g/100g
Fatty acids	GC-FID	0.001 g/100g
Vitamin D₃	HPLC-UV	1 µg/100g
B12	Microbiology	0.1 µg/100g
Selenium	ICP-MS	1 µg/100g
Iodine	ICP-MS	4 µg/100g

- **Contaminants: Description of the limit of detection (LOD) and the limit of quantification (LOQ) for dioxins and dioxin-like PCBs (dl-PCBs)**

For the analyses of dioxins and dioxin-like PCBs NIFES methodology is accredited according to ISO-standards and validated for using variable limit of detection (LOD) and limit of quantification (LOQ). LOD and LOQ are used to identify the lowest concentrations of an analyte (i.e. the congeners of dioxin and dl-PCB); the method can measure with accurate and reliable results. In this report the reported sum dioxins and dl-PCBs upper bound (UB) and lower bound (LB) values are based on variable LOQs determined for each congener in each sample (totally 29 congeners are included in sum dioxins and dl-PCBs). When determining low levels of organic pollutants in food and biological samples, the level of "noise" will increase relative to the "signal" as the concentration of the pollutant decreases. The noise will eventually be the limiting factor for the analytical method: Using a S/N ratio acquired close to the LOQ level, we define: $LOD = 3 * S/N$ and $LOQ = 10 * S/N$. When using a variable LOQ and LOD, the S/N ratio is determined for each analyte in each sample: In contrast, for a fixed LOD and LOQ the S/N ratio for each analyte is determined in a separate validation experiment.

Variable vs fixed LOD and LOQ; A theoretical basis for a fixed LOQ is that analysed samples is assumed to have similar analytical properties to the samples included in the validation experiment.

A variable LOQ may be applied in chromatographic analytical methods if sophisticated detector and soft-ware are used. Its theoretical basis is then that the instrumental signal (peak area) for each analyte contains a noise corresponding to the noise found immediately around the signal (peak area) of the analyte.

Procedure for variable LOD and LOQ: Each analyte's S/N ratio is automatically calculated from its surrounding noise, using standard deviation or optionally the mean peak area of the nearby chromatographic noise. Alternatively, the analyst may override this option and select

graphically a "typical peak area" in the surrounding noise. LOD is then $3 * S/N$ and LOQ is $10 * S/N$. Analyst intervention provides a more reliable LOD and LOQ, but is time consuming.

A variable LOQ is the limit of quantification achieved in the current sample. By using the S/N ratios from the current sample a lower LOQ value is often achieved, which is preferred when analysing contaminants where the goal is to quantify as low concentrations as possible.

Hannisdal et al. (2014) report the range of LOQ for each of the 29 dioxins and dl-PCB congeners for the farmed fish data used in this report. The range of LOQ of the congeners of dioxins and dl-PCBs data of wild fish used in this report is reported by Julshamn et al. (2010), Julshamn et al. (2007), Julshamn et al. (2013d), Nilsen et al. (2013a), Nilsen et al. (2010), Nilsen et al. (2012), Duinker et al. (2013) and Frantzen et al. (2009), Frantzen et al. (2010).

Appendix VII

Concentrations of nutrients and contaminants in fish used in the exposure estimates

In Chapter 6 of the main document, concentrations of nutrients and contaminants in fish and fish products on the Norwegian market are given in Tables 6.1-1, 6.2-1 and 6.3-1. However, choices have been made regarding which fish/fish products (presented in Chapter 6) to include in the calculations of nutrient intake and of contaminant exposure (presented in Chapter 7). Based on the reported fish consumed in one or several of the surveys (Chapter 3), data on nutrient and contaminant content had both to be available, and representative for fish on the Norwegian market. For example, Norwegian Spring Spawning herring (NVG herring) was used for the calculations since this herring population dominates the consumer market over the North Sea herring. For Atlantic cod, data on three populations are available (Chapter 6, Appendix V), i.e. coastal cod, North Sea cod and North East Atlantic cod. It is not possible to conclude that one population dominates the Norwegian consumer market over the others, and the contaminant and nutrient profile differ in the three. Hence, a mean nutrient and contaminant concentrations of the three cod populations were used to best represent the intake and exposure for consumers. Mackerel sampled in the North Atlantic was analysed for nutrients and contaminants. There are also available mackerel nutrient data of fish sampled in the North Sea (Chapter 6). These were not used for the calculations due to lacking contaminant data from the same population and very high mean fat content at 32 g/100 g fillet.

Nutrient and contaminant concentration data in farmed Atlantic salmon used for the calculations is the most recent analysed fish, i.e. sampled during 2013 and analyses finalised in 2014. Contaminant data on farmed trout from 2013 show very similar concentrations (Chapter 6), although analysed in far less samples compared to farmed salmon. Further, nutrient concentrations were not available for farmed trout from 2012 or 2013. Based on the very similar contaminant concentrations in farmed trout and salmon (Chapter 6) and similar changes in contaminant concentrations over time as observed in farmed salmon (Chapter 5), nutrient and contaminant concentrations in farmed salmon was used for the calculations for trout.

Concentrations of contaminants and nutrients of both wild halibut and wild Atlantic cod were used for the exposure and intake calculations, respectively. This was done since volumes of farmed cod and farmed halibut in Norway today is very low and negligible in the context of this report.

Nutrient and contaminant data of Atlantic cod roe was used to calculate the concentrations in caviar by using the percentage of roe in caviar. In surveys where intake data of fresh water fish was recorded, nutrient and contaminant concentrations of Perch were used for

exposure calculations. For consumers reporting eating fish liver, concentrations in cod liver was used for exposure and intake calculations.

The nutrient and contaminant concentrations for the fish species used for the intake and exposure calculations from fish can be found in tables:

- **Table AVII-1** Content of nutrients in fish fillet and fish products used in intake calculations in the main text
- **Table AVII-2** Concentrations of mercury (Hg) in fish and fish products used in exposure estimates in the main text
- **Table AVII-3** Concentrations of dioxins (PCDD), furans (PCDF), and dioxin-like PCBs used in exposure estimates in the main text

Table AVII-1 Concentrations of nutrients in fish fillet and fish products used in intake calculations in the main text

Food item	n	Year	Fat g/100g	Sum EPA, DPA, DHA mg/100g	Sum n-3 mg/100g	Sum n-6 mg/100g	Vitamin D µg/100g	Iodine µg/100g	Selenium µg/100g
Lean fish (≤ 5% fat)^a									
Atlantic cod, all populations ^{b,ABC}	51	2006/07/11	1.1	273	282	22	1.4 ^d	323	24
Saithe ^{c,B}	40	2006/11	1.4	439	458	27	1.4	160	30
Haddock ^{d,A}	-	-	0.6	No data ^e	No data ^e	No data ^e	0.7	No data ^e	28
Plaice ^{BC}	15- 20	2007	2.6	623	709	74	6.5	14	34
Redfish ^{d,B}	-	-	2.8	No data ^e	No data ^e	No data ^e	No data ^e	No data ^e	50
Wolffish ^B	3	2011	0.9	223	250	121	1.8 ^d	124	29
Tuna, canned ^{d,BC}	-	-	1	No data ^e	No data ^e	No data ^e	1.6	8	200
Fatty fish (> 5% fat)^a									
Atlantic halibut ^{f,B}	53	2005	2.3	612	709	80	12.0	18	No data ^e
Herring (Norwegian spring spawning) ^{g,BC}	30		9.9	1655	2213	170	14.5	2	58
Mackerel (North East Atlantic) ^{ABC}	10	2010	23.3	4456	6738	605	2.8	17	52
Atlantic salmon (wild) (Finnmark coast) ^B	99	2012	8.0	1765	2126	193	11.2 ^h	14 ^h	46 ^h
Atlantic salmon (farmed) ^{i,ABC}	90	2013	15.0	1311	2303	2296	7.5	4	12
Freshwater fish									
Perch ^{d,C}	-	-	1.3	No data ^e	No data ^e	No data ^e	0.8	18	28
Sandwich spreads from fish									
Cod roe and liver pate ^{j,ABC}	-	2014	32.6	5500 (EPA+DHA)	6600	No data ^e	39.1 ^d	234 ^d	60 ^d
Cod roe ^{j,ABC}	5	2014	6.4	300 (EPA+DHA)	700	No data ^e	12.1 ^d	104 ^d	9 ^d
Cod liver ^{k,BC}	41	2006/07	58.8	11296	13477	1323	89.4	379	80

^aLean fish=fish with fat content below 2%, medium fatty fish=fish with 2-5% fat and fatty fish=fish with <5% fat, ^bMean of cod harvested in the Norwegian Sea 2006 (10 samples), Northern Sea 2011 (10 samples) and Barents Sea 2006 (20 samples) and 2007 (11 samples). For vitamin D, 42 samples were analysed, ^cMean of saithe harvested in the North Sea 2006, Barents Sea 2006 and 2011, Haltenbank 2006 (10 samples per harvesting), ^dValues according to

the Norwegian Food Composition Table, 2014, ^ezero is used in the calculations due to no data, ^fMean of 53 samples of halibut harvested in Norwegian Sea and North Sea in 2005, ^gMean of Norwegian spring-spawning herring from the Norwegian Sea in 2005 and 2010, and the North Sea 2005 (10 samples per harvest), but for iodine, 10 samples were analysed, ^hValues from wild Atlantic salmon, fillet (Sørfjorden, Vossolaks), n=27, ⁱMean of 90 samples farmed salmon harvested in 2013, except for analysis of vitamin D where 70 samples were analysed, ^jValues from the food industry, 2014, ^kMean content in cod liver from cods harvested in the Barents Sea in 2006 (21 samples) and 2007 (10 samples) and in the Norwegian Sea in 2006 (10 samples).
A Values used in Småbarnskost 2007 (2-year-olds), **B** Values used in Norkost 3 (adults; 18-70 years of age), **C** Values used in MoBa (pregnant women).

Table AVII-2 Concentrations of methylmercury (Hg) in fish fillet and fish products used in exposure estimates in the main text

Food item	Year	n	Mean mg Hg/kg wet weight	
			Lower bound	Upper bound
Lean fish (\leq 5% fat)^a				
Atlantic cod, all populations ^{ABC}	2009-2011	2109	0.075	0.075
Saithe ^B	2010-2012	1620	0.051	0.051
Haddock ^{b,B}	2003	25	0.08 ^b	0.08
Plaice ^{BC}	2007	156	0.07	0.07
Redfish ^B	2007	178	0.13	0.13
Wolffish ^B	2003	10	0.021	0.025
Tuna, canned ^{BC}	2006	6	0.10	0.10
Fatty fish ($>$ 5% fat)^a				
Atlantic halibut ^B	2006-2010	88	0.26	0.26
Herring (Norwegian spring spawning) ^{BC}	2006-2007	800	0.039	0.039
Mackerel (Northeast Atlantic) ^{ABC}	2007-2009	845	0.039	0.039
Atlantic salmon (wild) ^B	2012	98	0.036	0.036
Atlantic salmon (farmed) ^{ABC}	2013	132 ^c	0.014	0.014
Freshwater fish				
Perch ^{d,c}	1965-2008	>5000	0.328	0.328
Sandwich spreads from fish				
Cod roe and liver pate ^{e,ABC}	2014	9	0 ^f	0.011
Cod roe ^{e,BC}	2014	unknown	0 ^f	0.011
Cod liver ^{BC}	2009-2011	1908	0.042	0.045

^aLean fish=fish with fat content below 2%, medium fatty fish=fish with 2-5% fat and fatty fish=fish with <5% fat, ^bOld values from the Seafood database, NIFES, and no data on lower bound exists, thus, for calculating purposes upper bound value are used as a conservative lower bound value, ^cPooled samples of five fish each, ^dValues from Jenssen et al. (2012), ^eData from the food industry, ^fzero is used due to values under limit of quantification (LOQ).

A Values used in Småbarnskost 2007 (2-year-olds), **B** Values used in Norkost 3 (adults; 18-70 years of age), **C** Values used in MoBa (pregnant women).

Table AVII-3
the main text

Concentrations of dioxins and dioxin-like PCBs used in exposure estimates in

Food item	Year	n	Sum dioxins ^a and dl-PCB ^b pg 2005-TE/g wet weight	
			Lower bound	Upper bound
Lean fish (≤ 5% fat)^c				
Atlantic cod (all populations) ^{ABC}	2007-2010	136	0.035	0.056
Saithe ^B	2006	41	0.072	0.097
Haddock ^B	2003	7	0.045	0.054
Flatfish, plaice ^{BC}	2007	25	0.33	0.34
Redfish ^B	2004	24	0.60	0.61
Wolffish ^B	2003	10	0.49	0.49
Tuna, canned ^{BC}	-	-	No data ^d	No data ^d
Fatty fish (> 5% fat)^c				
Atlantic halibut ^B	2006-2010	90	4.3	4.4
Herring (Norwegian spring spawning) ^{BC}	2006-2007	799	0.56	0.63
Mackerel (Northeast Atlantic) ^{ABC}	2007-2009	791	0.63	0.87
Atlantic salmon (wild) ^B	2012	92	0.82	0.96
Atlantic salmon (farmed) ^{ABC}	2013	102 ^e	0.4	0.5
Freshwater fish				
Perch ^{f,c}	-	-	No data ^d	No data ^d
Sandwich spreads from fish				
Cod roe and liver pate ^{g,ABC}	2014	9	4.3 ^h	4.3
Cod roe^{f,BC}	2005	4	0.321	0.321 ⁱ
Cod liver^{BC}	2009-2011	528	20.9	21.7

^aDioxins - PCDD/PCDF - polychlorinated dibenzo-para-dioxins (PCDD) and polychlorinated dibenzo furans (PCDF), ^bdl-PCB = dioxin-like PCB (non-ortho and mono-ortho substituted PCBs), ^cLean fish=fish with fat content below 2%, medium fatty fish=fish with 2-5% fat and fatty fish=fish with <5% fat, ^d zero is used in the calculations due to no occurrence data, ^ePooled samples of five fish each, ^fData from Kvaalem et al. (2009), ^gData from the food industry, ^hNo data on lower bound, for calculating purposes upper bound value are also used as a conservative lower bound value, ⁱ No data on upper bound, for calculating purposes lower bound value are used.

A Values used in Småbarnskost 2007 (2-year-olds), **B** Values used in Norkost 3 (adults; 18-70 years of age), **C** Values used in MoBa (pregnant women).

Concentrations of nutrients and contaminants in fish oil/cod liver oil used in the exposure estimates

For intake estimates of nutrients and exposure calculations from fish oil and cod liver oil, respectively, data for fish oil and cod liver oil were combined, and a weighed mean based on data from Tables 6.1-2 and 6.3-2 were calculated. Data for sum dioxins and dl-PCBs without lower bound were excluded since both lower and upper bounds were calculated. Overview of the data used can be found in tables below:

Table AVII-4 Concentrations of nutrients in fish oil/cod liver oil used in intake calculations in the main text

Supplement	Year	n	Fat %	Mean sum EPA+DPA+DHA mg/100g	Mean sum n-3 mg/100g	Mean vitamin D µg/100g
Cod liver/fish oil	2007-2011	21	100	28243	33797	134

Table AVII-5 Concentrations of dioxin and dl-PCB in fish oil/cod liver oil used in exposure estimates in the main text

Supplement	Year	n	Sum dioxins and dl-PCBs pg 2005-TEQ/g	
			Lower bound	Upper bound
Cod liver/fish oil	2011-2014	27	0.27	0.95