Health effects of nutrients and environmental pollutants in Baltic herring and salmon: a quantitative benefit-risk assessment

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Abstract

Background Dioxin health risks from fish remains a complex policy issue. Especially fatty Baltic fish, such as herring and salmon, contain relatively high concentrations of pollutants although they are otherwise healthy food. We studied the health benefits and risks of Baltic herring and salmon in four countries to identify critical uncertainties and to facilitate evidence-based discussion on the dioxin policy related to these fishes. Methods We performed an online survey about consumers' fish consumption and its motivation in Denmark, Estonia, Finland, and Sweden. Dioxin and methylmercury concentrations were estimated based on Finnish data. Exposure-response functions about several health endpoints were evaluated and quantified based on scientific literature. We also quantified infertility risk of men based on a recent European risk assessment about childhood dioxin exposure and its effect on sperm concentration later in life. Results Baltic herring and salmon contain e.g. omega-3 fatty acids and vitamin D, and the beneficial impact of these fishes on cardiovascular, mortality, and depression risk clearly outweighs risks of dioxins and methylmercury in people more than 45 years of age and in young men. The critical population subgroup is young women, who may expose their children to pollutants during pregnancy and breast feeding. However, the study suggests that even in this group the health benefits are larger or similar than health risks. Value of information analysis demonstrated that the remaining scientific uncertainties are not large. In contrast, several critical uncertainties are value judgements by nature: whether Baltic fish should be seen as primary or secondary source of nutrients; whether exceeding tolerable intake is an adverse outcome as such; and whether subgroup-specific restrictions are problematic or not. Conclusions Potential health risks from dioxins in Baltic fish have decreased to less than a half in ten years. The new risk assessment by European Food Safety Authority clearly increases the fraction of population exceeding the tolerable dioxin intake, but quantitative estimates of net health impacts change only marginally. Increased use of small herring (with less pollutants) is a no-regret option. Further value-based policy discussion rather than research is needed to clarify useful actions related to dioxins in fish.

Background

Dioxins (polychlorinated dibenzo-*p*-dioxins and furans) and polychlorinated biphenyls (PCBs) are persistent environmental pollutants that are found at relatively high concentrations in fish.[1] Fatty Baltic fish (notably Baltic herring, salmon, trout and lamprey) biomagnify dioxins and PCBs in the food chain and constitute the largest exposure source of these compounds in e.g. the Finnish population.[2] These fish species often exceed the EU limits for dioxins and PCBs[3], but Finland and Sweden have a permanent derogation to sell these fish species on national market; Latvia has derogation for salmon[4]. For example Estonia deals with dioxins by selecting human food from small Baltic herring with lower concentrations[5].

The EU has had a long-term objective of reducing human exposure to these pollutants. Emission standards for industry have become stricter during the last decades, and also concentration limits for food and feed have eliminated the most contaminated items from the market. Although average exposure has decreased to a fraction of previous values, there is still concern about health effects of dioxins, especially related to fatty fish in the Baltic Sea.

European Commission therefore asked European Food Safety Authority EFSA to perform a risk assessment and derive an updated tolerable weekly intake (TWI) for dioxins and dioxin-like PCBs. The TWI was recently published, and it is seven times lower (2 pg/kg/week) than the previous value (14 pg/kg/week)[6].

Although there are previous benefit-risk assessments about Baltic fish[7], there were no studies that would have compared several countries and studied reasons and motivations for fish eating (or fish avoidance).

BONUS GOHERR project (2015-2018) looked at the particular question about dioxins in Baltic salmon and herring and performed a health benefit-risk assessment, which is reported here. The project also studied biological, socio-economic, cultural, and food security aspects of the dioxin problem of Baltic salmon and herring fisheries and the governance of the dioxin problem.

Methods

Modelling

The overall aim of the study was to estimate health risks and benefits of important compounds (dioxins, dioxin-like PCBs, methylmercury, omega-3 fatty acids [consisting of eicosapentaenic acid EPA and docosahexaenic acid DHA], and vitamin D) found in Baltic herring and salmon in the current situation. The assessment model was implemented in an open and modular way at Opasnet web-workspace (en.opasnet.org). In practice, this means that all the data and code used for different parts, or modules, of the model are located on different pages at Opasnet. These pages are called knowledge crystals, as their structure and workflow follow certain rules (Tuomisto et al 2019, forthcoming). In this section, we give an overview of the model and describe the input data and assumptions used; the Result section consists of model results. Links to the module pages and all details can be found from the assessment page[8]. The whole model with data and codes is available on the page and also at Open Science Framework research data repository[9].

The benefit-risk assessment was based on a modular Monte Carlo simulation model, which had a hierarchical Bayesian module for estimating dioxin concentrations. The different modules are briefly described below, with references and links to further material.

The input distributions were derived either directly from data or from scientific publications. If no published information was available (as was the case with e.g. disability weights for non-typical endpoints such as tolerable weekly intakes or infertility), we used author judgement and wide uncertainty bounds (these judgements are described later in the text). The model was run with 3000 iterations using R statistical software (version 3.5.3, https://cran.r-project.org).

Consumption survey

The data used were from an internet-based survey that was conducted at the end of 2016. The survey focused on consumers' eating habits of Baltic herring and salmon in four Baltic Sea countries: Denmark, Estonia, Finland, and Sweden (Figure 1). The questionnaire was designed and the results analysed by the authors, but the survey was administered by a professional market research company Taloustutkimus oy, which has an established internet panel since 1997. The survey company recruited over 500 consumers from each country (total 2117) to respond to the survey questionnaire, which is above the required sample size to generalise the results to each case study country (with a 95% confidence level and 5% margin of error)[10]. The survey was targeted to adult population, i.e. 18 years or older.

The survey questionnaire comprised 32 questions, including sociodemographic questions as well as questions relating to fish consumption frequency and amount in general, and to Baltic herring and salmon in particular. There were also questions about reasons to eat or to not to eat those species, and policies that may affect the amount eaten. The questionnaire was translated into the national language of each case study country (Finnish, Swedish, Estonian and Danish). The country and gender of the respondents were provided directly by the internet panel and were therefore not included in the questionnaire.

Only those respondents who reported fish consumption in general were asked follow-up questions about herring and salmon consumption, and are included in the analysis presented in this paper. As the survey focused specifically on consumption of herring and salmon originating from the Baltic Sea, a distinction had to be made in the questionnaire between Baltic herring and herring originating from elsewhere, e.g. the North Sea or North Atlantic, as well as between the salmonids (Baltic and Norwegian salmon, farmed salmon, rainbow trout). Regarding herring consumption, the respondents that reported eating some type of herring were asked explicitly whether they consume Baltic herring. Concerning Baltic salmon, the respondents were asked to choose from a list of salmonids, which ones they consume. The survey was designed and conducted for the purposes of this study and another study about consumer perception and consumption. The latter study[11] was published first, and it contains a more detailed description of the study methods, including the questionnaire.

Individual long-term fish consumption (in kilograms per year) was estimated from consumption frequency and amount questions. Consumption distributions were produced for subgroups defined by country, gender, and age by random sampling (with replacement) of the individual estimates. People's reactions to changes in policies or fish market (e.g. what if fish consumption is recommended or restricted; what if the availability and usability of these species improves; what if the price of fish changes) were predicted based on their answers. These decision scenarios were used to alter the business-as-usual scenario and compare results between scenarios.

Also a few technical scenarios were developed: what if nobody ate either fish more than ca. 1 kg per year; and what if fish is considered a primary versus a secondary source of nutrients. The latter scenario is important if dose-responses are non-linear, as is the case with vitamin D where the benefits occur only if exposure exceeds the recommended daily value. In such a case, the incremental health benefits of a primary source may differ from those of a secondary source.

The data analysis was conducted using R software (version 3.5.3, http://cran.r-project.org). Because the survey was conducted on an internet panel rather than on a random sample from the general population, the respondents may not be fully representative of the actual population distributions of the countries. Therefore, the respondents were weighted based on actual age, gender, and region distributions of each country to produce population representative results.

To support transparency, the anonymised data and all the results will be available online:
http://en.opasnet.org/w/Goherr:_Fish_consumption_study

Concentrations

Fish-size-specific PCDD/F and dioxin-like PCB concentration distributions for each fish species and country were estimated based on EU Fish II study[12]. The results were based on pooled and individual fish samples (98 Baltic herring and 9 salmon samples) and analysed for 17 dioxin and 37 PCB congeners. A hierarchical Bayesian module was developed with the JAGS package of R software. The model assumed ca. 7 per cent annual decrease in dioxin concentrations, based on long time trends measured in Finland. The fish samples were caught between 2009 and 2010.

The concentrations in Baltic herring were found out to be highly sensitive to fish size, while size-dependency was much weaker in salmon. Herring sizes in different scenarios came from a fish growth model developed in BONUS GOHERR project[13].

The fish samples came mostly from the Bothnian Sea, which is an important area for Finnish and Swedish catch. The concentration distributions for the studied countries were derived from the concentration model results by scaling them with the average concentration on a catch area of interest relative to the average from the Bothnian Sea. The Danish and Estonian catch areas were assumed to be Baltic west of Bornholm and the Gulf of Finland, respectively. The Swedish catch areas for herring and salmon were assumed to be the Baltic Main Basin and the Bothnian Sea and Bay, respectively. The area selection was based on landing statistics provided by the International Council for the Exploration of the Sea (ICES)[14][15].

Dioxin and PCB concentrations were weighted and summed up to toxic equivalency quantities (TEQ) by using WHO 2005 toxic equivalency factors (TEF)[16]. Levels of fatty acids and vitamin D in Baltic herring were based on measurement data obtained from the Finnish Food Safety Authority, and those in salmon are based on Fineli food database[17]. Methylmercury concentrations were based on Kerty database[18].

Exposures

Exposures to pollutants and nutrients were simply products of consumption amounts as assessed from the survey and concentrations in the consumed fish, with possibly an uncertain background intake from other sources. An exception to this were the infant's exposures to dioxins and methylmercury during pregnancy and breast-feeding, as they were derived from the mother's exposure using toxicokinetic models.

Infant's exposure during pregnancy and breast-feeding was estimated with this equation:

$$C_{s,i} = \frac{I_{a,m} * t_{1/2,m} * f_m * FE}{ln2 * BF_i},$$

where $C_{s,i}$ = serum (s) concentration of dioxins in the infant (i) in pg/g fat; $I_{a,m}$ = average daily intake of dioxins of the mother (m) in absolute (a) amounts pg/day; $t_{1/2,m}$ = the half-life of dioxins in the mother (2737.5 d = 7.5 a); f_m = fraction of ingested dioxins actually absorbing from the gut in the mother (0.80); FE = fraction of mother's dioxin load that is transported to the infant during breast feeding (0.25); BF = body fat amount in the infant (into which the dioxins are evenly distributed) during the period when tooth and testis are sensitive to defects and the exposure at its highest (ca. six months of age) (1 kg)[19]

Exposure-responses

Several benefits and risks were assessed (Table 1). We tried to choose impacts that are arguably large enough that could affect the benefit-risk balance. Effects of omega-3 fatty acids on coronary hear disease mortality and child's intelligence, as well as vitamin D effects on vitamin deficiency belong to this category. In contrast, there are several endpoints that have been linked to fish or omega-3 intake, but they were not included because current evidence is controversial: diabetes[20], prostate cancer[21], asthma[22], and stroke[23].

In addition, many studies have linked health benefits to fish consumption rather than a specific nutrient[24]. We included depression[25], breast cancer[26], and all-cause mortality[27], because the results have been fairly consistent in meta-analyses. In summary statistics, CHD and breast cancer mortalities were subtracted from all-cause mortality to avoid double-counting.

The dioxin effect on sperm concentration[6] and methylmercury effect on child's intelligence[28] are the most sensitive risks of these pollutants, and they were therefore included.

In addition, we included some other dioxin effects. Tolerable weekly intakes from 2001 and 2018 were included for comparing methods of quantitative benefit-risk assessment (based on a single health aggregate, DALY) and more qualitative benefit-risk assessment (based on assessing whether a beneficial or harmful threshold is exceeded). Cancer effect was included because the news media often refers to dioxins as "the super poison causing cancer" even if researchers have thought for years that developmental rather than cancer risks are more relevant; a quantitative assessment could give guidance to news communication. And finally, tooth defects were included because it is a sensitive dioxin endpoint, but no study has compared its magnitude to sperm effects. Interestingly, some of the key papers of this effect had studied Finnish mothers, which had been exposed to dioxins mostly from Baltic herring[29][30][2].

The exposure-response function of methylmercury was a synthesis of EFSA tolerable weekly intake and a linear function from Cohen et al.[31]. This was necessary because although the EFSA estimate is fairly recent, it does not quantify the magnitude of effect if the TWI is exceeded. The function by Cohen was based on concentrations measured from mothers' hair. A conversion from hair concentrations to daily exposures was performed according to U.S.EPA[28].

Table 1. Exposure-response functions used in the assessment.

Exposure agent	Response	Esposure-response unit	Exposure-response function mean (95 % confidence interval)	References and notes
TEQ (intake through placenta and mother's milk)	male infertility due to sperm concentration decrease	pg /g in boy's body fat	linear; slope 0.00006 (-0.000019, 0.00014)	Based on EFSA TWI assessment[6]. Mother's exposure must be converted to child's exposure (measured as pg /g fat)[32]
TEQ (intake through placenta and mother's milk)	developmental tooth defects	log (pg /g) in child's body fat	linear; slope 0.0014 (0.00029, 0.0025)	epidemiological study in Finland[29]
TEQ	cancer morbidity	pg/kg/day	linear; slope 0.00051 (0.000026, 0.00097)	U.S.EPA dioxin risk assessment[33].
TEQ	tolerable weekly intake 2001	pg/kg/week	acceptable range below 14	EC Scientific Committee on Food recommendation[34]
TEQ	tolerable weekly intake 2018	pg/kg/week	acceptable range below 2	EFSA recommendation[6]
omega-3 fatty acids	coronary heart disease mortality	mg/day	ED50: -0.17 (-0.25, -0.091)	Cochrane review[23]
vitamin D	vitamin D recommendation	µg/day	acceptable range 10 - 100	a step function based on the daily intake recommendations for adults in Finland[35]
ALA	coronary heart disase mortality	mg/day	RR 0.95 (0.72 - 1.26)	after 1000 mg/d of alpha-linolenic acid intake; Cochrane review[23]
omega-3 fatty acids	breast cancer	mg/d	RR 0.95 (95% CI 0.90, 1.00)	after 0.1 g/d of marine omega-3; a meta-analysis[26]
fish	all-cause mortality	g /d	RR 0.88, (95%CI 0.83, 0.93)	after 60 g/d of fish; a meta-analysis[27]
fish	depression	g/d	RR 0.83 (95% CI 0.74, 0.93)	after 35 g/d of fish; a meta-analysis[25]
methylmercury	loss in child's IQ points	mg/kg/day	linear; slope 6.6 (-0.27, 14)	a synthesis of EFSA TWI estimate[36] and a previous risk assessment[31].
DHA	loss in child's IQ points	mg/day	linear; slope -0.0013 (-0.0018, -0.00081)	a previous risk assessment[37].

We derived the exposure-response functions for infertility and tooth defects indirectly from published results, so the rational of those endpoints is described here in more detail.

In humans, sperm concentrations have been shown to decrease permanently if boys are exposed to dioxins before nine years of age. The data come from Seveso[38][39] and a Russian children's study[32].

EFSA recently assessed this risk from the Russian children's study and concluded that significant effect was seen already in the second quartile with median PCDD/F TEQ concentration 10.9 pg/g fat, when measured from the serum of the boys at the age of ca. 9 years. Mean sperm concentration was ca. 65 (95 % CI 50-80) million/ml in the lowest quartile, while in all other quartiles the concentration was ca. 40 (95 % CI 30-55) million/ml. Due to the shape of the effect, we used a non-linear exposure-response curve with half of the maximum effect (effective dose 50, ED50) occurring at TEQ concentration 10 pg/g fat.

However, sperm concentration as such is not an adverse health effect. It only manifests itself if the concentration is low enough to prevent conception in a reasonable time window, say, five years. According to a review, the success rate of couples who try to get pregnant is 65 % in 6 months if the sperm concentration is above 40 million/ml[40]. Below that concentration, the probability is fairly proportional to the sperm concentration.

Based on this, we estimated that (assuming independent probabilities between 6-month periods), the probability of not getting pregnant in five years follows this curve:

P(infertility after 5 a) = (1 - 0.65 (1+ (-0.39c)/(c + 10 pg/g)))^10,

where c is the dioxin concentration in boy's fat tissue. This curve is pretty linear below TEQ concentration 50 pg/g with slope ca. 0.00006 g/pg, meaning that for each 1 pg/g increase in dioxin concentration the boy's fat tissue (or serum fat), there is an incrementally increased probability of 0.00006 that he cannot get a child even after five years of trying.

Exposure-response function for tooth defect was also derived from several studies. Alaluusua and coworkers have studied dioxin exposure in small children and the development of permanent molar teeth. They have found defects in both general population in Finland from the exposures in the 1980's [29] [30] and children exposed during the Seveso accident[41].

Based on these studies, we approximated that the effect is linearly correlated with the logarithm of the dioxin concentration in the child.

Disease burden

Disease burden[42] was estimated in one of two alternative ways (Figure 2): if an exposure agent affects the burden of a particular disease in relation to the background of the disease, the attributable fraction of a particular compound exposure was calculated. If the relation was not relative to background, the attributable number of cases due to the exposure was estimated, and this was multiplied by the years under disease per case and the disability weight of the disease (Table 2.).

$BoD_i = BoD * PAF_i = BoD * f * (RR_i - 1) / (f * (RR_i - 1) + 1)$, or

$BoD_i = N_i * L * Dw = P * f * UR_i * E_i * L * Dw$,

where BoD is the burden caused by the disease under study, i is an exposure agent affecting the risk of the disease, PAF is population attributable fraction, f is the fraction of population that is exposed, RR_i is the relative risk that the population faces due to the studied level of exposure to exposure agent i (as compared with a counterfactual scenario with no exposure), N_i is the number of disease cases attributed to exposure agent i, L is the duration of a disease incident, Dw is the disability weight of the disease (0=perfect health, 1=death), UR is the absolute unit risk, and E is the exposure to the agent.

Table 2. Case burdens of different health responses. Case burden is calculated as the product of disease-specific disability weights and disease durations.

Response	DALYs per case	Description
tooth defect	0 - 0.12	disability weight 0.001 and duration 60 a with 100 % uncertainty. For comparison, IHME gives disability weight 0 for asymptomatic caries and 0.006 for mild other oral disorders with symptoms[43].
cancer	19.7 (17.8 - 21.8)	based on breast cancer, from IHME[44]
vitamin D intake	0.0001 - 0.01	disability weight 0.001 and duration 1 a with 100-fold log-uniform uncertainty
TWI 2001	0.0001 - 0.01	disability weight 0.001 and duration 1 a with 100-fold log-uniform uncertainty
TWI 2018	0.0001 - 0.01	disability weight 0.001 and duration 1 a with 100-fold log-uniform uncertainty
infertility	0-5	disability weight 0.1 and duration 50 a with 100 % uncertainty. See also text. Here we used a clearly higher disability weight than IHME (0.008)[43].
child's IQ	0.11 (95 % CI 0.06 - 0.16)	Mild intellectual disability (IQ<70) has disability weight 0.043 (95 % CI 0.026-0.064) based on IHME[43]. This is scaled to one IQ point with duration 75 a.

Background disease burdens were needed for all-cause and coronary heart disease mortality, as well as breast cancer and depression; they were obtained from the Institute for Health Metrics and Evaluation (IHME) (Table 3.)[45]. Disease burden of a cancer case was based on IHME data. Also disability weights of diseases were based on their estimates, if available. Duration estimates of diseases were mostly based on the time window considered (one year) or lifetime (in the case of permanent infertility, tooth or IQ effects due to infant exposure). We tried to be realistic with estimates but also not to underestimate the risks of fish consumption, so that potential conclusions about safety of fish would not be unfounded.

With the non-typical health effects, namely exceeding tolerable weekly intakes and deviation from the vitamin D recommendation, we used very wide uncertainty distributions, as it was unclear how much weight should be given to endpoints that are only indications of potential health risk rather than actual adverse effects. A value of information analysis was performed to test the importance of these uncertainties.

Childlessness can be viewed as tragedy of life, so the disability weight could be in the order of 0.1 DALY per year permanently (50 years). However, the disability weight applies to only half of the children (boys). Therefore, we used 0.1*50*0.5 DALY/case = 2.5 DALY/case, with rather high uncertainty (0-5 DALY/case).

Population data for each country for year 2016 was available from Eurostat database. Data was separated for gender and age (18 – 45 years and > 45 years) groups[46].

Table 3. Total burden of disease of selected causes from all risk factors in the study countries[44].

Disease	1000 DALYs per year, mean (95 % CI)			
	Denmark	Estonia	Finland	Sweden
Breast cancer	20 (11, 30)	3.9 (2.5, 5.6)	16 (10, 23)	30 (18, 42)
Depression	21 (18, 25)	7.6 (6.4, 8.8)	33 (27, 38)	62 (51, 73)
Heart (CHD)	84 (79, 88)	54 (47, 61)	150 (140, 160)	200 (190, 210)
Mortality	810 (780, 840)	250 (240, 270)	800 (770, 830)	1200 (1180, 1250)
Vitamin D intake	2.1 (0.11, 9)	0.5 (0.026, 2.1)	2.1 (0.11, 8.8)	3.7 (0.19, 16)

Value of information analysis

Value of information is a mathematical method that compares the difference of utility (money, DALYs or other measure of the objective) in two scenarios: that some additional information is obtained before a decision is made, or that the decision is made with the current information. This can be formulated as

$$VOI = E(\max_i(U(d_i))) - \max_i(E(U(d_i))),$$

where VOI is value of information, E is expected value, U is the utility of decision d, and i is an index of decision options[47]. In this study, we also estimated the value of including or excluding an option to the decision making.

Results

Concentration distributions of the key exposure agents in Baltic herring and salmon are shown in Figure 3. Baltic herring has lower concentrations than salmon for most exposure agents studied, but for vitamin D the levels in salmon are lower. Dioxin concentrations have reduced a lot since 1970, and the trend since 1990 is shown in Figure 3.

Fish consumption varies a lot between countries and population subgroups, and also within each subgroup (Figure 4.). There is large individual variation (almost hundredfold) in fish consumption within most subgroups.

Only about a quarter of people report any wild Baltic salmon consumption. Many people also say that they do not know where their salmon comes from and whether it is salmon or rainbow trout. Herring consumption is more accurately known, although the Danes are not sure whether their herring comes from the Baltic Sea or the North Sea. For example, in Finland a typical dish name contains the word *herring* (*silakka* in

Finnish), if it contains Baltic herring. Therefore the species is often known to the consumer even if the dish is not self made. However, this is not true with Baltic salmon.

There is also large variation between population subgroups. Estonians eat clearly more Baltic herring and Danes eat less than individuals from other countries. Males tend to eat more, and young people eat less than other population subgroups. These differences are rather similar in all countries, although at different levels. The fraction of people that do not eat Baltic herring at all varies remarkably between subgroups: it is only 25 % in old male Estonians, while it is more than 90 % in young female Danes. There is also a sizable fraction who eat Baltic herring more than 3.6 kg/year (10 g/day). This varies from a few percent in young people to up to ca. 30 % in old Estonians.

The average consumption of Baltic herring and salmon is 1.4 and 0.5 kg/a per person, respectively, in Finland according to estimates based on our survey. However, the Natural Resources Institute Finland reports (mostly based on landing statistics) that the consumption of Baltic herring and salmon were 0.31 and 0.07 kg/a per person, respectively[49]. This implies that people tend to overestimate their long-term average consumption in general and for Baltic salmon in particular. Because of this discrepancy, we performed a sensitivity analysis where our consumption estimates in our assessment were scaled to match the Finnish statistics (data not shown). The results of all variables were smaller, but the overall picture remained the same. Also, a notable fraction of population still exceeded the TWI 2018 value.

We also asked in the questionnaire, how the respondent would change fish intake if an increase or decrease of fish consumption was recommended by authorities (Figure 5.). The outcome depends on previous consumption but not much on population subgroup. If increase is recommended, a clear and systematic increase is seen in the average response. In contrast, a recommendation to reduce intake results in inconsistent effects. Some people would follow the recommendation, but almost an equal number would not, and most would not change fish intake. This phenomenon is seen already at current intake levels below 1.8 kg/year, where most of the population is.

Because of the large variation in fish consumption, also the dioxin exposure from Baltic fish varies more than hundred-fold within population subgroups (Figure 6.). The variation between subgroups is also large. In the model, many people have apparent zero exposure because other dioxin sources than Baltic fish were not included. A fraction ranging from a few percent to a quarter exceed the EC Scientific Committee on Food TWI value from 2001[34]. The fraction is much higher, from 20 to up to 75 %, when the new EFSA TWI value of 2 pg/kg/week from 2018 is used as the criterion[6].

The main objective of this study was to compare health risks and benefits of Baltic fish consumption. The most dominant feature are the health benefits from all-cause mortality, ischemic heart disease, and depression (Table 4). Figure 7. shows a large variation between population subgroups. In old age groups, they clearly outdo all risks. In most population subgroups, the benefits are typically much larger than risks. In contrast, the risks and benefits in young women are both small, but at individual level, risks are often larger according to the model.

Table 4. Burden of disease related to Baltic herring and salmon consumption.

Response	Exposure agent	DALYs per year, mean (95 % CI)			
		Denmark	Estonia	Finland	Sweden
Cancer (all)	TEQ	160 (0, 1300)	57 (0, 370)	150 (0, 1300)	260 (0, 2200)
Cancer (breast)	Omega-3	-310 (-3700, 0)	-55 (-450, 0.002)	-130 (-1400, 0)	-330 (-4000, 0)
Child's IQ	DHA	-88 (-1000, 0)	-180 (-1300, 0)	-58 (-370, 0)	-540 (-7600, 0)
Child's IQ	MeHg	390 (0, 1900)	170 (0, 1100)	56 (0, 270)	370 (0, 6100)
Depression	Fish	-130 (-1200, 0)	-79 (-430, 0)	-170 (-1300, 0)	-420 (-3000, 0)
Heart (CHD)	ALA	3.1 (-220, 290)	-20 (-150, 37)	-40 (-560, 280)	-47 (-880, 510)
Heart (CHD)	Omega-3	-190 (-2600, 200)	-120 (-1400, 69)	-300 (-2300, 120)	-530 (-7300, 820)
Infertility	TEQ	110 (0, 1100)	66 (-23, 410)	44 (0, 470)	75 (0, 460)
Mortality	Fish	-2200 (-20000, 0)	-1200 (-8300, 0)	-2800 (-21000, 0)	-5600 (-44000, 0)
Tooth defect	TEQ	160 (0, 2400)	38 (0, 170)	11 (0, 130)	34 (0, 480)
TWI 2001	TEQ	400 (0, 6000)	87 (0, 1400)	180 (0, 2400)	460 (0, 6100)
TWI 2018	TEQ	690 (0, 7400)	310 (0, 2100)	660 (0, 5700)	1000 (0, 12000)
Vitamin D intake	Vitamin D	-88 (-490, 0)	-42 (-340, 0)	-59 (-420, 0)	-200 (-1800, 0)

Figure 8. shows several different objectives that could be used as a basis for decision making. The first one is using net health effect, estimated like in the quantitative benefit-risk assessment performed here. The second objective focusses only on young women as the target group facing the risks, and ignores impact to others. Third and fourth objectives try to avoid exceeding tolerable weekly intake values from 2001 and 2018, respectively.

When the whole population is considered (left bar), net health objective recommends increasing rather than decreasing Baltic fish consumption in every country, while TWI approaches suggest that reducing fish consumption is a better option. If only the target population of young women is considered (second-left bar), all impact values are close to zero, but net health impact may sometimes show slightly larger risk than benefit; the situation is ambiguous but stakes are not high.

Health impacts overall are much smaller in young age groups, and in young women the critical issues are effects on their children's intelligence quotient (IQ), tooth defects, and sperm concentration, not the health impacts on the woman herself. These risks emerge due to dioxin and methylmercury exposures during pregnancy and breast feeding. Child's own diet during early years may also have an impact, although the exposure then is typically much lower. These risks are in the same range as the health benefits, and the overall balance depends mostly on the disability weights of distinct outcomes and other value judgements such as whether Baltic fish is considered as a primary source of nutrients.

Based on our survey, a policy of recommending increased consumption seems to be somewhat effective, while a recommended consumption reduction is indistinguishable from the business-as-usual scenario. In contrast, factual actions to reduce dioxin emissions and consequently exposures have been very effective during the last 40 years (see Figure 3 for concentration trends).

In a bigger picture, dioxins in Baltic herring and salmon are only one of the many environmental health hazards (Figure 9.). They cause smaller risk than methylmercury from fish, and their risk is not even close to the largest health risks originating from air pollution (which may be up to tens of thousands DALY in Finland alone); but it may be in the top 10 list.

It is possible that we are overoptimistic about the current sperm concentrations, as reduction from subfertile background levels could increase the probability of infertility more than our model predicts. So, we did a sensitivity analysis on men with decreased sperm concentrations from an unrelated reason. Dioxins are likely to reduce that even further. For example, if the sperm concentration is 10 million/ml, the probability of infertility in five years is 0.32 based on the equation above. That increases to 0.4 at dioxin concentration 10 pg/g. If ten percent of the population had such low semen concentration and if 20 % of boys exceed 10 pg/g (as seems to be the case according to our model), then we would see for example in Finland 25000 boys/year * 0.1 with low fertility * 0.2 with high dioxin * 0.08 absolute increase in infertility = 40 cases per year, each 2.5 DALY and thus 100 DALY in total. This is more than the 29 DALY from the default model, but does not change the overall picture in Figure 9. Individual risk per mother would be 0.1 and 0.03 mDALY/a per person, respectively (compare to Figure 7). They are also much smaller than the 25000 boys/year * 0.1 with low fertility * 0.32 absolute probability of infertility * 2.5 DALY = 2000 DALY due to infertility from all other causes of low sperm concentration in our sensitivity analysis.

IHME estimates the disease burden of male infertility of all causes at only 52 DALY/a in Finland, and the value including female infertility is roughly a double of that[44]. So, it seems that our estimates seem to overestimate rather than underestimate the sperm concentration problem.

Value of information was looked at for specific decision scenarios, where a group of similar decisions were considered together.

Value of information was calculated for the total burden of disease in a random study country (Denmark, Estonia, Finland, and Sweden were not weighting by population), but using uncertainties for individual people. This approach ensures that value of information is not underestimated, because at population level many uncertainties average out and are smaller than at individual level.

Decision about selecting herring size has practically no expected value of perfect information (less than 1 DALY/a for a whole country) because switching from large to small herring is a no-regret option and in most cases better than other alternatives.

Decision about consumer policy (including improved information, better availability and usability of fish, and consumption recommendations) has expected value of perfect information of 150 DALY/a, so there is some uncertainty about what to do. The maximum net benefit is usually achieved by increasing Baltic fish intake. Therefore, the most important decision option to include in the decision process is to increase information and fish availability (there would be expected loss of 1600 DALY/a if that option was not considered).

The analysis was also performed for the young female subgroup separately, assuming a situation where subgroup-specific policies are plausible and effective and do not affect other subgroups. The expected value of perfect information was 190 DALY/a. At the same time, the total disease burden at stake is clearly smaller than with the whole population (see Figure 7), because disease burden from overall mortality and heart disease are small among young women. These two results together show that the uncertainties about what to do with respect to young women are clearly larger than with other subgroups.

Discussion

Dioxin and PCB concentrations have been constantly decreasing in Baltic fish for 40 years, and now they are mostly below the EU limits. Also Baltic herring consumption has been decreasing during the last decades and is now less than a kilogram per year, varying between age groups (old people eat more), genders (males eat more) and countries (Estonians eat more and Danes less than other countries studied). People reported that better availability of easy products, recipes, and reduced pollutant levels would increase their Baltic herring consumption[11]. In contrast, recommendations to reduce consumption would have little effect on average.

According to this study, health benefits of Baltic herring and salmon clearly outweigh health risks in age groups over 45 years. Benefits are similar to risks in the most vulnerable subgroup, women at childbearing age. The balance depends on value assumptions: risks prevail if exceeding the tolerable weekly intake (especially the new 2018 value) is given weight in the consideration; but benefits are larger if other omega-3 sources are considered secondary to Baltic fish. The analysis was robust in the sense that we did not find factual uncertainties that could remarkably change the conclusions and would warrant postponing decisions in hope of new crucial information.

The largest health benefits come from reduced all-cause mortality, coronary heart disease, breast cancer, and depression, and improved intelligence quotient of the child of a woman consuming fish. Each of these effects have been linked to either fish in diet or more specifically to omega-3 fatty acids, implying that a full palette of benefits is not available from food supplements only.

Methylmercury risk on child's IQ appeared as large or even larger than all dioxin risks combined (Table 4), although a common belief is that dioxins are the largest risk with Baltic fish. In addition, dioxin cancer risk was much smaller than risk of infertility despite the reputation of dioxins as carcinogens.

There seems to be room for updated risk communication. This analysis suggests that dioxins are not the largest health risk related to Baltic fish; and that dioxin cancer risk is small in everyday life. The facts that dioxins are very potent per microgram of substance and that they cause cancer in laboratory animals after high doses[1] are irrelevant details in risk communication and rather give a wrong impression of the actual health risks.

We found some no-regret policies. Promoting the consumption of small Baltic herring rather than large ones brings all health benefits but reduces exposure to pollutants. Promoting Baltic fish to other population subgroups than young females brings more health than harm. And reducing dioxin emissions to atmosphere will reduce concentrations in fish as well as in dairy and meat products.

One critical question about this assessment is whether the beneficial effects are actually real and causal. The recent Cochrane review concluded that there is little if any cardiovascular benefit from omega-3 supplements[23]. Aung et al. conducted a meta-analysis of omega-3 supplement trials with more than 77000 individuals[50]. They found only weak, border-marginal cardiovascular benefits and concluded that the study did not support the use of dietary omega-3 supplements. The US NCCIH says more about these studies and also: "Moderate evidence has emerged about the health benefits of eating seafood. The health benefits of omega-3 dietary supplements are unclear."[51].

Indeed, omega-3 supplements may not affect diet composition, but each fish meal replaces another meal of some kind. These other dietary changes complicate estimates on the impacts of a specific nutrient. Therefore, it is warranted to look at epidemiological meta-analyses on fish consumption as a whole. Fish consumption had clear beneficial effects on all-cause mortality[27] and depression[25]. In contrast, marine omega-3 fatty acids, but not fish consumption, was linked to reduced risk of breast cancer[26]. It seems plausible that not all effects are mediated specifically via omega-3 fatty acids, but that fish likely has several beneficial nutrients and makes a part of healthy diet where it is difficult to point out any one compound as the source of benefits.

Elizabeth Pennisi reports several studies about the genetic variation of fatty acid metabolism and its links to cardiovascular risk[52]. The overall conclusion is that although these issues are not well understood, there seems to be genetic variation about the health benefits of omega-3 fatty acids. Lauritzen et al. made a review on docosahexaenoic acid (DHA) and concluded that it is especially important for the developing brain during fetal period and infancy, although there may be variation in intrinsic production and therefore in the need of DHA from food. [53] Also this implies variation within the population.

In any case, several beneficial effects from fish make the case stronger: even if one endpoint turns out to be less important than previously thought, as has recently happened with omega-3 supplements and cardiovascular health, it is still unlikely that all of them are false positive. In this assessment, we used the Cochrane best estimate of omega-3 effect, which was described as "little, if any use for cardiovascular disease prevention". Interestingly, the benefit was still larger than the dioxin risks from the same fish. This result emphasises the importance of quantitation and context: what is small depends on the comparison.

A previous benefit-risk assessment was performed on omega-3 fatty acids and dioxins[54]. The study found scenarios where consumption of herring in the Netherlands would bring benefits of omega-3 but dioxin exposure would remain below the tolerable intake of the time (14 pg/kg/week).

Another study concluded that Atlantic herring provides cardiovascular health benefits at consumption levels where the dioxin cancer risk remains acceptable[55]. Also a Chinese study concluded that herring containing PCB7 concentrations 12.5 ng/g fresh weight can be used regularly and get health benefits without significant contaminant risks[56]. This equals approximately 2-3 pg/g fresh weight of TEQ, assuming that PCB7/TEQ ratio is similar in Finnish and Chinese herrings.

However, The National Food Agency of Sweden published a report with a conclusion that increased herring consumption would unnecessarily increase dioxin risks, while it is possible to eat fish with less dioxins (e.g. smaller herring) and gain the same health benefit[57]. The report did not assess how consumption would change in practice, if Sweden abandoned the exemption to use large herring.

None of these benefit-risk assessments compared the magnitude of risks and benefits quantitatively on a common scale such as DALY. A more common approach is to compare exposure estimates from a study to an administrative threshold. Clear conclusions can be made if risks are below and benefits above their respective thresholds, or vice versa. However, the approach gives little advice in situations where there is need for quantitative comparison of risk and benefits.

A threshold-type exposure-response function leads to, according to our experience, tendency to use the threshold as a strict guideline for action. This leads to inefficient allocation of resources, as it is unlikely that the risks would abruptly increase or benefits decrease.

A quantitative benefit-risk assessment attempts to estimate the total benefits and total risks and then compare those. This results in a need to estimate all relevant endpoints, even if there is uncertainty about the mere existence of a causal effect. There is a reason for this need: if an uncertain endpoint is rejected from further scrutiny, mathematically it implies certainty about zero impact. Therefore, it is necessary to avoid omissions and try to produce a balanced quantitative view of both risks and benefits on the one hand, and of their uncertainties on the other hand.

This is also important for risk communication and risk perception. If all hazards are just "risky" or "not risky", people fail to learn that some risks are worse than others. For example, our whole fish benefit-risk assessment comes to an illustrative light when compared with other major environmental health risks: maybe it is not worth worrying too much if bigger risks are ignored. Having said that, it should be remembered that even small risks are worth reducing if the costs of reduction are low or even negative.

The recent EFSA TWI recommendation for dioxins (2 pg/kg/week as compared with the previous TWI 14 pg/kg/week) dramatically increases the fraction of non-compliant population in all countries studied. However, the implications of this fact are far from clear and require further discussion. We encourage both researchers and administrators to pay much more attention to comparing risks and benefits instead of only considering risks isolated from real, complex situations[58]. Our results raise several questions.

First, the most sensitive outcome, namely sperm concentration decrease, is only relevant for young women whose future children may be affected. Should the TWI still be applied to all population subgroups?

Second, as dioxin exposure strongly relates to diet consisting of otherwise healthy Baltic fish (especially Baltic herring) in the Nordic countries, should these health benefits be considered when dioxin policy is designed? For example the Swedish food safety authority did not raise this issue in their commentary about the new EFSA TWI[59].

Third, Baltic herring has also other important values than health: economic (Baltic herring is the most abundant catch species by weight in the Baltic Sea), ecological (sustainable yield of Baltic herring is large and the catch removes nutrients from the sea), climate (Baltic herring could replace red meat and other climate-unfriendly food sources), social (Baltic herring is inexpensive local food), and cultural (Baltic herring and salmon are an important part of coastal culture)[60][61]. Moreover, Baltic herring has value for food security[62][5][11]. Should these values be considered when dioxin policy is designed? BONUS GOHERR project found that all of these issues are considered important in the society[63][64].

The results of the study should not be considered as exact magnitudes of the properties studied. We attempted to quantify actual, measurable properties but acknowledge that these are just humble estimates of the actual truth, sometimes produced with few data. We also tried to use probability distributions systematically to reflect our ignorance and also actual variation in populations. We had to make several assumptions about e.g. actual impacts of policies, how representative Finnish measurements are for fish in other countries, what background exposures to use, and how to derive disability weights or durations. In any case, we had to convert all outcomes into a single metric for policy and value-of-information analyses, and DALY seemed to be usable. We had to stretch the definition slightly to include non-disease outcomes, and we also had to use author judgement to estimate the impacts of competing risks, which are not directly observable from epidemiological data. Previous assessments have shown large health benefits related to fish, so when under uncertainty, we tried to be realistic but also tried to avoid underestimating risks, because that bias might weaken arguments about safety of fish.

We have made the data, code, and reasoning available at Opasnet to facilitate the work of potential critics to find mistakes and false interpretations and also offer a place to publish critique. A quantitative benefit-risk assessment can actually be seen as one step in an iterative process, where the understanding improves in an interaction with assessments and researchers, resulting in updated assessments in the next steps. Quantitative benefit-risk assessments would offer material for substantive discussions about making informed compromises between risks and benefits.

This study was not designed to answer value-based questions but it was able to identify some. The value of information was low for the remaining scientific uncertainties about dioxin risks, and the critical questions are such as the value questions mentioned above. Of course, dioxin sources and concentrations vary in different parts of Europe and the world, but because of biomagnification, fish is a typical source of many persistent pollutants everywhere. Political discussion and deliberation is needed about risk-benefit comparisons. Scientific facts are crucial, but not the only crucial, elements in that discussion.

Conclusions

In conclusion, despite the new evidence and the new EFSA TWI recommendation, this study suggests that Baltic fish is still safe and healthy food for most population subgroups in the Nordic countries. A special subgroup, namely young women planning to have children, is of special concern. Their health benefits are smaller than in older age groups, and also there are potential risks to the child that is exposed during pregnancy and breast feeding. Experts do not agree on conclusions about this subgroup, but the scientific uncertainties actually do not play a large role. In contrast, value judgements are crucial when designing policies for the dioxin problem of Baltic fish. These questions should be carefully discussed and deliberated among decision makers, experts, citizens, fishers, and other stakeholders.

Abbreviations

CHD: coronary heart disease

CI: confidence interval

DALY: disability-adjusted life year

DHA: docosahexaenoic acid

ED50: effective dose 50

EFSA: European Food Safety Authority

EPA: eicosapentaenoic acid

IHME: Institute for Health Metrics and Evaluation

IQ: intelligence quotient

ICES: International Council for the Exploration of the Sea

MeHg: methylmercury

TEF: toxic equivalency factor (of dioxins)

TEQ: toxic equivalency quantity (of dioxins)

TWI: tolerable weekly intake

WHO: World Health Organisation

Declarations

Ethics approval and consent to participate

An online survey was performed to adult consumers in Denmark, Estonia, Finland, and Sweden by Taloustutkimus Ltd. We asked about fish eating habits but not about health or other sensitive issues. We did not ask or collect identity information of the respondents, except age, gender, and country, which were used for classification in analyses. The survey did not involve any interventions. Due to these reasons and according to the national guidelines, there was no need for ethical approval. (National Advisory Board of Research Ethics. Ethical principles of research in the humanities and social and behavioural sciences and proposals for ethical review. Helsinki; 2009. https://www.tenk.fi/sites/tenk.fi/files/ethicalprinciples.pdf. Accessed 24 Sept 2019.) The consent to participate was obtained from the study participants in writing.

Consent to publish

Not applicable.

Availability of data and materials

The whole benefit-risk assessment was performed online at http://en.opasnet.org/w/Goherr_assessment, and all details (including data, code, results, descriptions, and discussions) are openly available, except for the personal data from the consumer survey. The consumer survey data was converted to and published as synthetic data, i.e. data that does not represent any real individuals but that has similar statistical properties as the actual data.

The datasets generated and analysed during the current study, together with the other material mentioned above, are available at Open Science Framework research data repository by the Centre for Open Science. https://osf.io/brxpt/

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

JT planned the assessment design, performed most of the analyses, and wrote the first draft of the manuscript based on input from other authors. PH coordinated the project and participated in designing and linking of this work to other parts of the project. AA designed and performed the questionnaire study. PM participated in the discussions about the design and interpretation of results. All authors read and approved the final manuscript.

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Authors' information

No specific information.

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Figures

Figure 1

Countries where the BONUS GOHERR consumption survey was performed. Source: Europe with Countries - Single Color by FreeVectorMaps.com

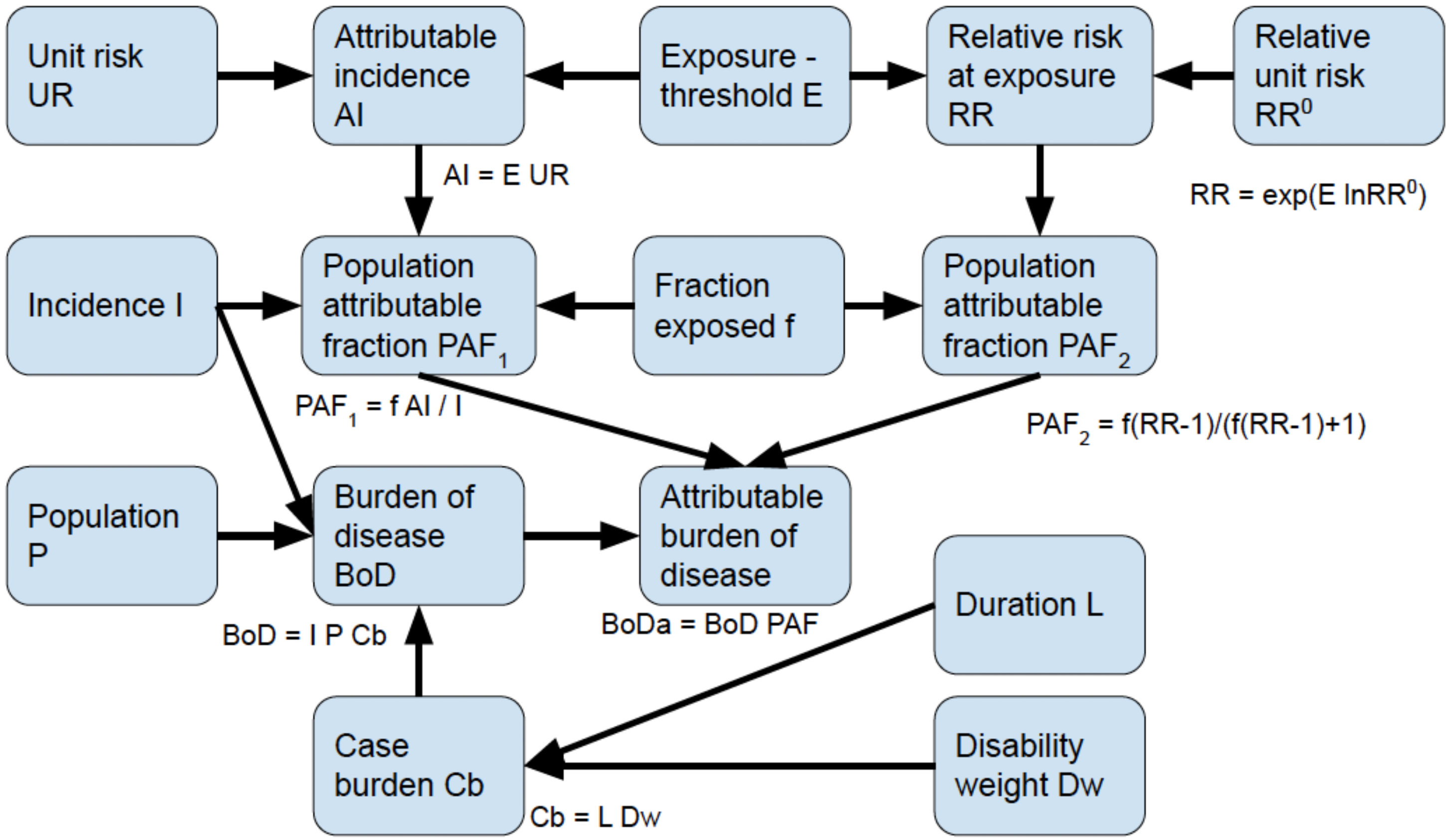

Figure 2

Schematic diagram of the health impact assessment model used. Each blue node is a submodel, and arrows are functional relations. The main equation of the relations is shown beside each node.

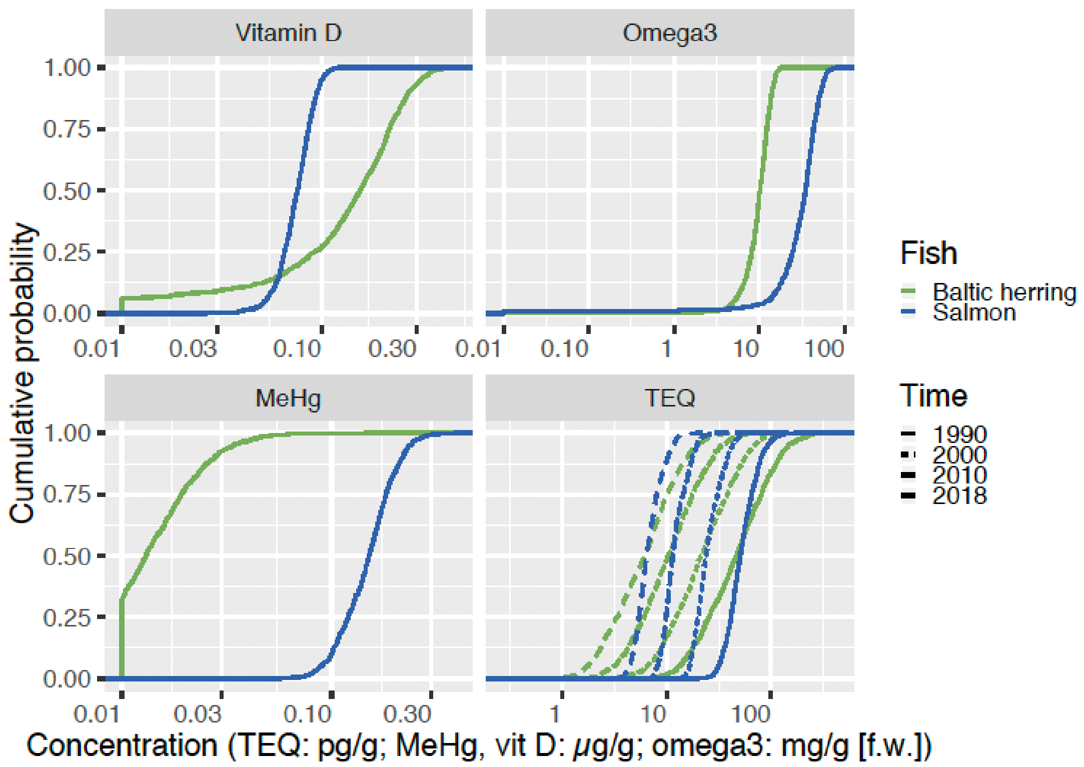

Figure 3

Cumulative concentration distributions of the four key exposure agents in Baltic herring and salmon. For dioxin, also the decreasing time trend since 1990 is shown. Caption: Concentrations of compounds in Baltic fish

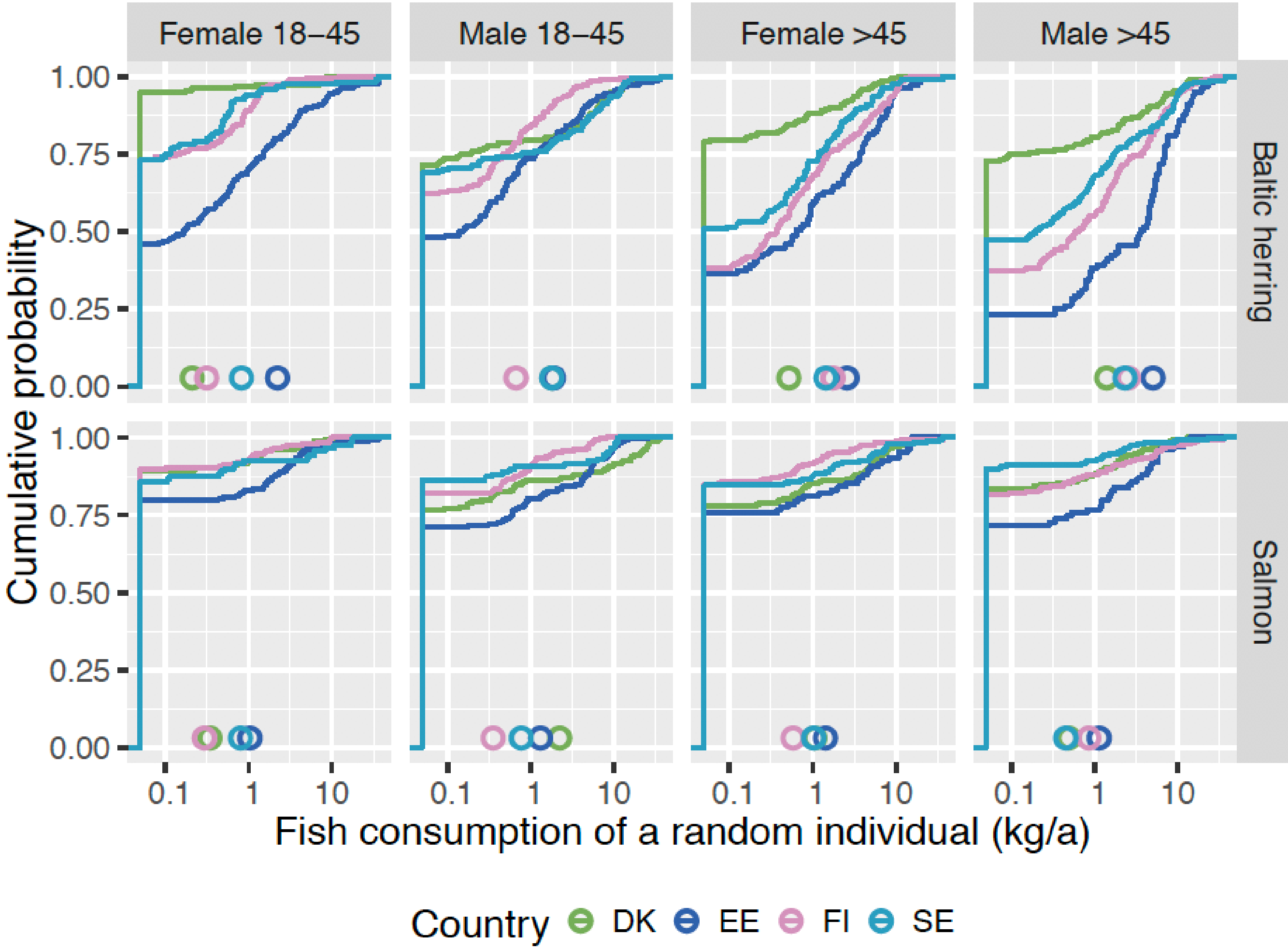

Figure 4

Cumulative fish consumption distributions of Baltic herring and salmon in different subgroups of the studied countries. The mean of each distribution is shown with a circle. Caption: Consumption of Baltic fish by country and subgroup

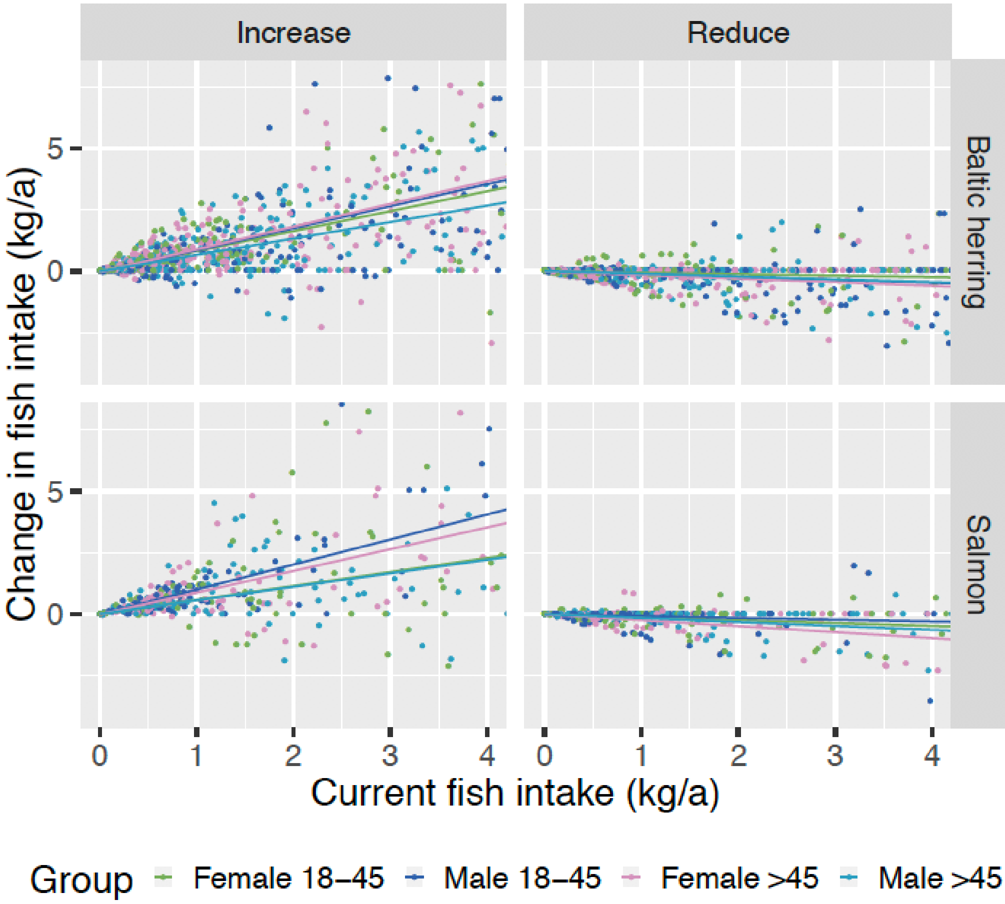

Figure 5

Individual change in consumption after policies to either increase or reduce fish intake. Caption: Individuals' fish intake after all consumption policies

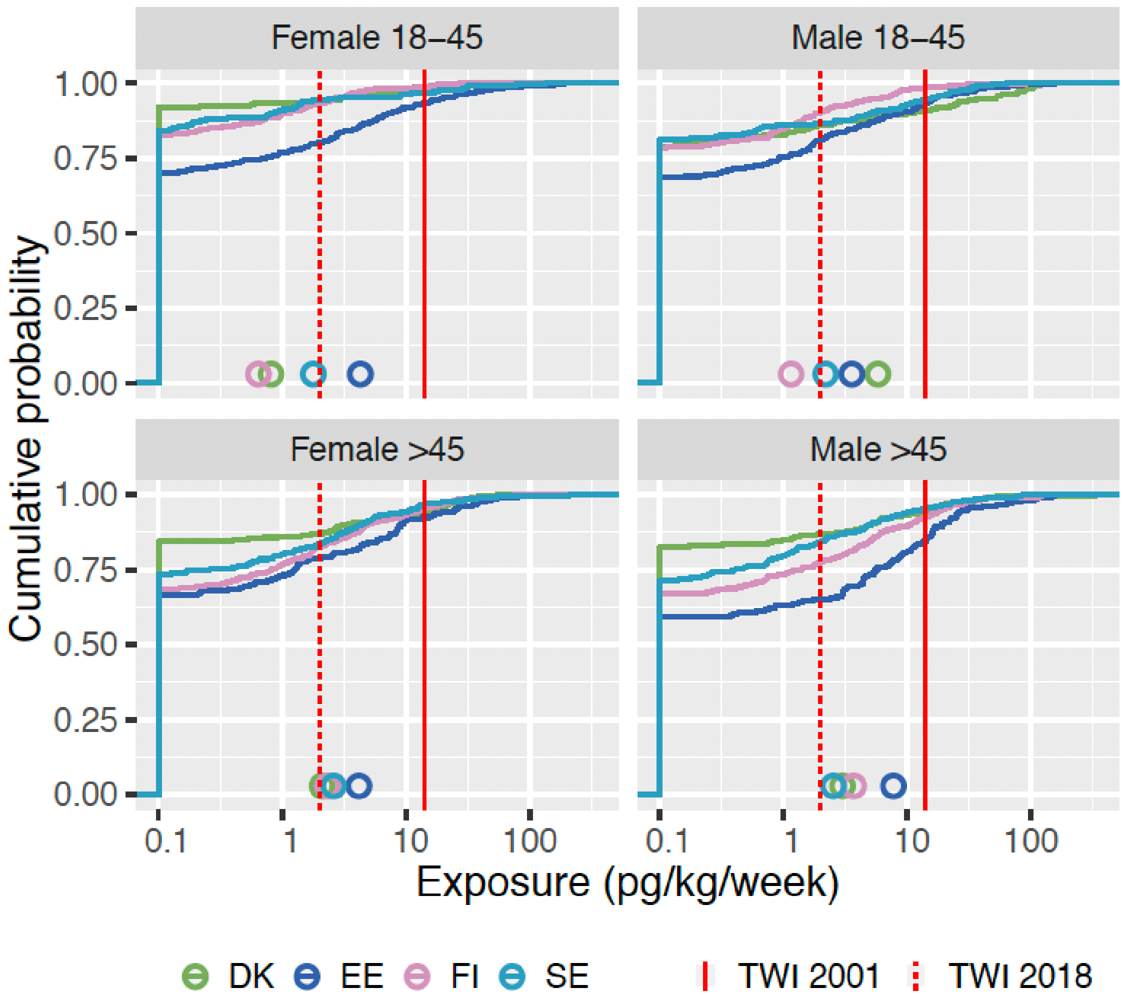

Figure 6

Cumulative dioxin (TEQ) exposure distributions shown by subgroup and country. The mean of each distribution is shown with a circle. Caption: Exposure to dioxins from Baltic fish

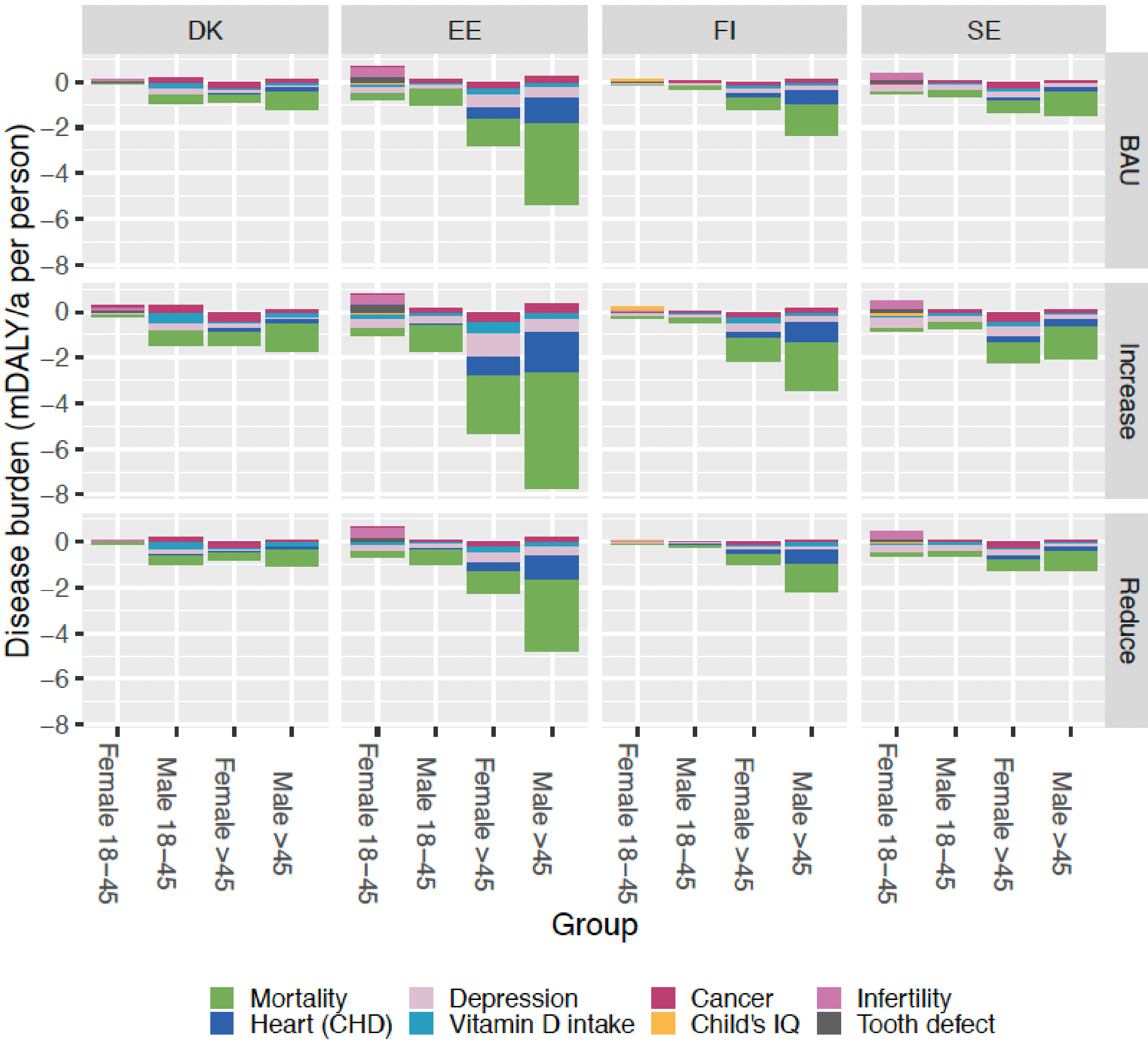

Figure 7

Disease burden attributable to eating Baltic fish in Denmark, Estonia, Finland, and Sweden (expected value at individual level). Note that negative values mean improved health. mDALY: 0.001 disability-adjusted life years, CHD: coronary heart disease, IQ: intelligence quotient. Caption: Disease burden attributable to Baltic fish by country, group, and policy

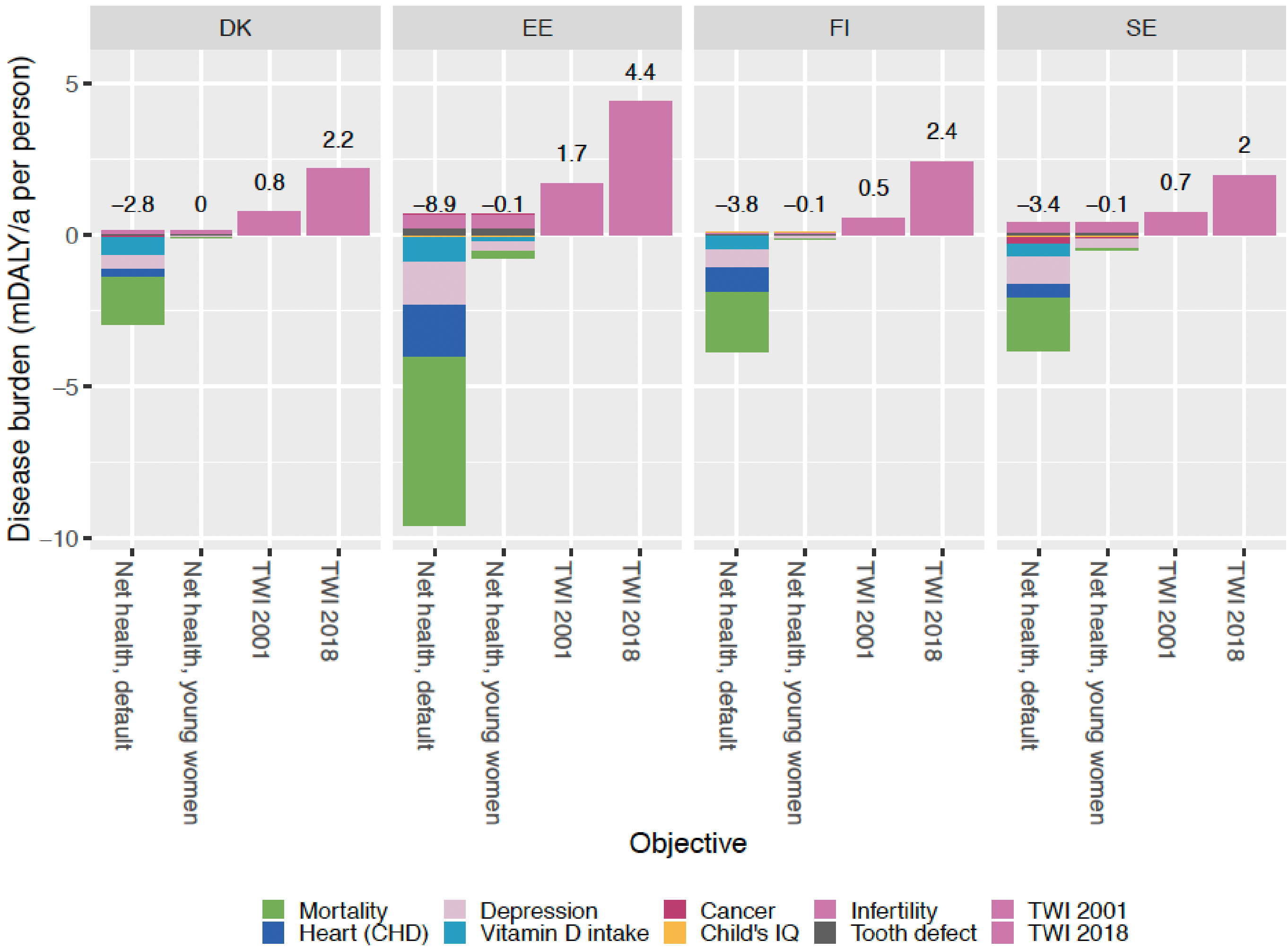

Figure 8

Outcome of interest using different objectives. The default objective (the main assessment of this article) focusses on total net health effect in the whole population. The second objective focusses on young women only. Tolerable weekly intakes from 2001 and 2018 are converted to DALYs based on the number of people exceeding the guidance value. Caption: Disease burden using different objectives

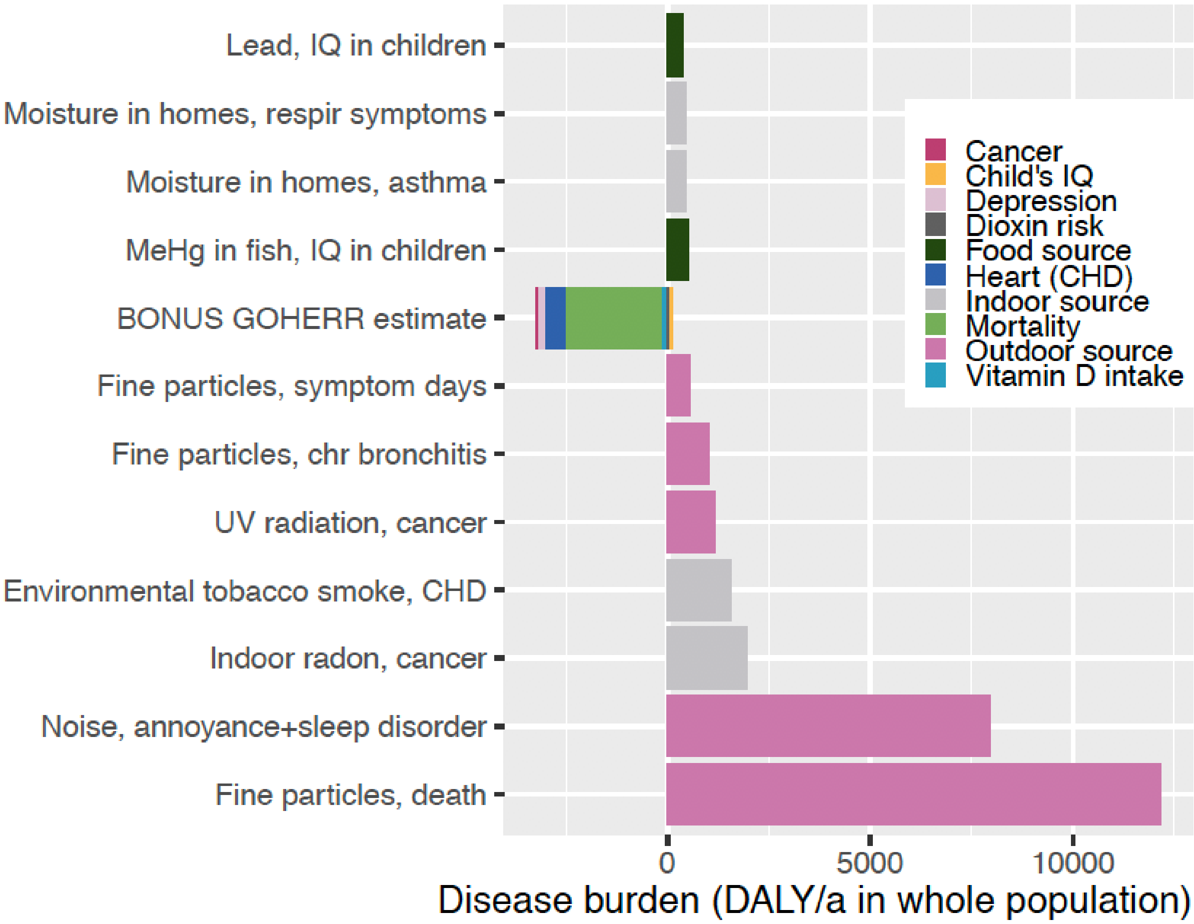

Figure 9

Burden of disease of the most important environmental health factors in Finland. BONUS GOHERR results are from this study, others from a previous publication[48]. Caption: Environmental disease burden in Finland