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Risk-benefit assessment of five underutilized fish species in Norway

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ABSTRACT

Risks and benefits of increasing the consumption of five underutilized demersal fish species in Norway by applying the Benefit-Risk Analysis for Foods (BRAFO)-tiered approach were assessed. A reference scenario with zero intake was opposed to two different alternative scenarios of 250 (AS1) and 450 g (AS2) per week. Health-benefit vs. health-risk calculations were computed. Moreover, tolerable weekly intake and recommended weekly intake were considered for the general public and women of childbearing age. In addition, the molar ratio of Selenium and Mercury (Se:Hg) and the Health Benefit Value of Selenium (HBV_{Se}) were calculated and considered. Results suggest that a consumption of 250 g, when combined with a weekly portion of fatty fish, is the optimal intake scenario for adequate polyunsaturated fatty acids. Flounder and megrim feature the significantly highest eicosapentaenoic+doxosahexaenoic acid values with 678 and 606 mg in AS1. A surplus of selenium was detected in all five species, with flounder and lemon sole showing significantly highest Se:Hg (21; 22). Moreover, no detrimental effects were found due to an increased contaminant intake among those eating fish. Consequently, results revealed a net beneficial health effect by increasing the consumption of the five underutilized fish species. Thus, their consumption can be recommended.

1. Introduction

The health effects of fish and seafood are widely known and appreciated, and the main attributed beneficial effects are due to high amounts of proteins and long-chain polyunsaturated fatty acids (LC-PUFAs). In fact, fish and seafood contain satisfying amounts of important LC-PUFAs that promote physiological, molecular as well as cellular processes (Calder, 2014). Nevertheless, when consuming fish, possible exposure to environmental and chemical contaminants must be considered. Methylmercury (MeHg) is the primary form of mercury found in foodstuffs and due to its high toxicity, regulations for the maximum concentration have been established. The European Commission set a maximum level for fish and fishery products of 0.5 mg/ kg (wet weight) (EC, 2006). Moreover, the European Food Safety Authority (EFSA) Scientific Panel on Contaminants in the Food Chain (CONTAM) prompted a tolerable weekly intake (TWI) for MeHg of 1.3 μg/ kg body weight (b.w.) (EFSA, 2012a). Seafood is the primary source of human MeHg intake and is known to be neurotoxic and to cause oxidative stress, due to its interactions with sidechains of proteins and non-proteins (Farina et al., 2011). The antagonistic relationship between MeHg and Selenium (Se) has been recognized previously, but it is not yet completely certain which metabolic pathways are predominantly responsible for the high toxicity of MeHg (Khan and Wang, 2009). On the other hand, a constant supply of Se is required to synthesize vital selenoenzymes, which are essential for shielding the brain tissues from oxidative stress. Therefore, an adequate intake (AI) of 70 μg/ day was established by EFSA (2014) Moreover, fish can also be a source of dioxins and polychlorinated biphenyls and need to be considered when consuming fish, as contaminants can lower the beneficial effects from LC-PUFAs amongst others (Sofoulaki et al., 2019) Therefore, risk-benefits assessments (RBA) can be applied to assess the net beneficial vs. detrimental health effects of consuming foodstuffs. RBAs are valuable tools for authorities and governments to give guidelines on safe consumption of certain foodstuffs. As reviewed by Thomsen et al. (2021) RBA is a useful tool to assess the health impact of consumption patterns of fish and can help promoting the consumption of certain fish species. RBAs are heterogeneous in its nature, depending on if they are concluded for specific fish, consumer groups, in between different species or for specific countries. However, what they all have in common is the identification and comparison of beneficial and detrimental components and their consequences on human health. According to Thomsen et al. (2021) the minority of RBAs is conducted on fish consumption

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of a specific country whereas a majority of RBAs compares the risk-benefit of consuming different fish species or seafood products. Moreover, a majority of RBAs on fish and seafood focusses on eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and Se as beneficial components opposing them to MeHg, dioxins and dioxin-like polychlorinated biphenyls (dl-PCBs) (Afonso et al., 2013; Prato et al., 2019; Reyes et al., 2017; Sofoulaki et al., 2019; Strandberg et al., 2016).

Fish are an important food source for the Norwegian population, marked by a yearly per capita consumption of 31.5 kg of whole fish (round weight) and 13.3 kg of fillets (Norwegian Directorate of Health, 2022). However, Norwegian waters, being the second longest coastline worldwide, inhabit over 220 fish species, including species being so far underutilized and of minor commercial interest (Directorate of Fisheries, 2022). In particular, the five species considered in this study, European plaice (*Pleuronectes platessa*), megrim (*Lepidorhombus whiffiagonis*), European flounder (*Platichthys flesus*), lemon sole (*Microstomus kitt*), and thornback ray (*Raja clavata*), can be categorized as underutilized in Norway as partly described by Bjørklund, Henriksen. (2011). The European Commission (2020) announced that stocks of e.g. European plaice are moving further north and will possibly decline in the Northern sea, suggesting increasing stocks in the Norwegian sea. Since all five species are bottom-living fish and inhabit the same regions, these migration trends will be relevant for local fishermen in Norway. The previous study by Kendler et al. (2023) featured the favorable chemical and nutritional composition of the five demersal fish species, and also elaborates on micronutrient and contaminant levels. Moreover, Kendler et al. (2023) studied the seasonal effect on the chemical composition and contaminants of European plaice and Tsoukalas et al. (2022) looked into different packaging and storage conditions on the microbial and physiochemical quality of European plaice. However, no direct comparison between beneficial and health risk factors have been conducted up to date. To promote the consumption of these five underutilized fish species, it is important to consider both the potential health effects and risks that come with increased consumption. To our knowledge, no risk-benefit assessment on the consumption of those five species has been carried out. A recent report conducted by the Norwegian Scientific Committee for Food and Environment (VKM) as well as previous studies from VKM, focus on the risk assessment of the main consumed fish species in Norway, with limited and more general data on, e.g. European flounder and European plaice as no consumer data of these fish is available (Norwegian Scientific Committee for Food and Environment et al., 2022).

To our knowledge, no data on the specific consumption of the five species of interest has been collected in Norway up to date. Therefore, this study aimed to assess the net health effect of increased consumption of European plaice, European flounder, megrim, lemon sole and thornback ray originating from the west-coast of Norway. The objective was to establish recommendations for consuming these five underutilized fish species following the Benefit-Risk Analysis for Foods (BRAFO)-tiered approach.

2. Materials & methods

2.1. Scope of RBA study

The scope of this risk-benefit assessment lies purely on the five mentioned underutilized species, originating from the Norwegian west coast: European plaice, European flounder, megrim, lemon sole and thornback ray. The safety of different possible patterns of consumption has been evaluated, which can be reflected in recommendations for consumption for the Norwegian population of these fish. As this RBA focuses on fish originating from coastal waters on the west coast of Norway as the fishing region and the Norwegian adult population as the target group, existing data on species originating from, e.g. the Mediterranean sea or Northern sea were not considered in the assessment.

The focus of the study was on the general public and women of childbearing age for all intake calculations and the assessment of risks and benefits. Pregnant women were considered for calculations on possible IQ changes of infants in AS1 and AS2, but children below 18 years or elderly people above the age of 70 were not considered in this risk-benefit assessment.

2.2. Fish species and sampling

The fish species that were included in this RBA are five underutilized fish species in Norway, four flatfish (*Pleuronoectiformes*) and one belonging to the family of rays (*Rajiformes*). More precisely, individuals of European plaice (*Pleuronectes platessa*), flounder (*Platichthys flesus*), lemon sole (*Microstomus kitt*), megrim (*Lepidorhombus whiffiagonis*), and thornback ray (*Raja clavata*), were investigated. The sampling of the fish from two previous studies by Kendler et al. (2023) and Kendler et al. (2023) took place in autumn and winter 2020 as well as spring 2021 in the fishing area 2.a.2 as defined by (FAO, 1990–2021) along the west-coast of Norway. The sample size for each species was as following: n(flounder)= 7, n(lemon sole)= 5, n(megrim)= 5, n(plaice)= 10, n (thornback ray)= 5. During handling and processing of samples, the fish was constantly kept on ice and subsequently frozen at − 80 °C until further analysis. Due to its morphology, two sampling points for the four flatfish species (n= 2 ×2) and one sampling point for thornback ray were chosen, as visualized in the study by Kendler et al. (2023).

2.3. Sample analysis: consideration of results from previous studies

Kendler and co-authors have previously published results on nutritional composition, chemical and environmental contaminants as well as storage stability under different conditions on the five species of interest. Detailed information on the analyses of fatty acid distribution as well as essential trace elements and chemical and microbiological contaminants, can be found in the respective studies of Kendler et al. (2023); Kendler et al. (2023) and Tsoukalas et al. (2022).

For this study, values from e.g. fatty acids, selenium or mercury were re-calculated to be suitable for assessing benefits and risks (Section 2.5). Moreover, a literature review on contaminant and nutritional data of the five species of interest was carried out. The Marine Research Institute, Norway, obtained values of multiple contaminants in European plaice in a report on "Contaminants in plaice, anglerfish and pollack" (Frantzen et al., 2020). Those values were considered in the discussion part of the RBA.

2.4. Risk-benefit assessment methodology and approach

The BRAFO-tiered approach evaluates risks and benefits in a five-step process as previously presented by Boobis et al. (2013) and Hoekstra et al. (2012), and summarized by Nauta et al. (2020). This study attempted to follow this five-step assessment approach in a consecutive matter on the five species of interest, starting with the pre-assessment and problem formulation (step 1), which defines suitable intakes as a reference and alternative scenarios. Followed by tiers 1 and 2, containing the evaluation of the risk-benefit question (RBQ), including the individual assessment of risks and benefits (tier 1, step 2). If no benefits are detected, the consumption of the reference scenario can be advised. In contrast, the alternative intake scenario can be suggested if no additional risks go along with the respective alternative scenario. In both cases, the RBA can be stopped, and no further evaluation is necessary. In step 3 (tier 2), a quantitative integration of risks and benefits is carried out. In this step, the reference scenario is opposed to the newly proposed alternative intake scenarios. Here, either the reference or alternative scenario can be suggested if the benefits/ risks prevail over each other. In tier 3 (step 4), a quantitative comparison of risks and benefits is carried out by applying a deterministic computation with a common health metric (Hoekstra et al., 2012). This usually results in calculating Disability-adjusted life years values (DALYs) or Quality-adjusted life years (QALYs). The computation of DALYs or QALYs is only possible if sufficient consumption data or epidemiological data on the consuming population is available on the species of interest. As previously stated in the aims of the study, to our knowledge there is no intake data of the five species of interest available in Norway. That is why no exposure/ intake data of identified beneficial and detrimental components could be obtained from public studies. Consequently, this RBA was conducted with a qualitative approach, using analytical results from previous studies as a base on the intake of the specific nutrients/ contaminants. Furthermore, with no available consumption data of the five underutilized fish species, the study will follow the BRAFO-tiered approach from the pre-assessment and problem formulation, tier 1 until tier 2.

2.5. Pre-assessment and problem formulation

The Norwegian Directorate of Health (2011) recommends adult fish consumption of 300–450 g per week, of which 200 g should be obtained from fatty fish. In a recently published comprehensive general report on the assessment of benefits and risks of fish in the Norwegian diet from the Norwegian Scientific Committee for Food and Environment et al. (2022), alternative scenarios with 300 as well as 450 g fish intake were chosen. The study of the Norwegian Scientific Committee for Food and Environment included the general intake of fatty and lean fish, rather than recommendations for specific fish species, for the Norwegian public.

Therefore, a theoretical reference scenario (RS) with zero intake of the five species was selected and followed in the assessment. As alternative scenario 1 (AS1), a weekly intake of 250 g of the five fish species of interest was chosen. Together with the suggested intake of 200 g fatty fish by the Norwegian Directorate of Health (2011), AS1 would lead to a total of 450 g fish per week, suggesting that the 250 g is covered by one of the five species as a source for lean fish. As alternative scenario 2 (AS2), a weekly intake of 450 g for the five lean fish species was chosen to assess whether the consumption of 450 g consisting of at least one of the five fish species is reasonable in terms of benefits and risks connected to its consumption, or not. Moreover, whether AS2 is sufficient in providing eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), usually associated with the intake of fatty fish. In this study, the intake of fatty fish was not assessed, but it was expected that 200 g fatty fish are consumed additionally to the 250 g as proposed in AS1. Moreover, the focus of the assessment lies purely on the possible risks and benefits of an increased consumption (AS1 vs. AS2) of the five lean fish and does not include any potential risks/ benefits through additional fish consumption.

This leads to the following three scenarios that were compared in this study:

1. Reference scenario (RS): no consumption of the five species, which refers to the current intake, assuming no frequent consumption of these fish. The current weekly intake data assessed from the Norwegian Scientific Committee for Food and Environment et al. (2022) was used.
2. Scenario 1 (AS1): consumption of 250 g fish/ per week, assuming that the suggested consumption of 250 g lean fish per week by the Norwegian Directorate of Health (2011) is fulfilled by consuming the five species in the study. Additionally, the Norwegian Directorate of Health (2011) suggests the intake of 200 g fatty fish. The calculations for AS1 are conducted for the 250 g portion of lean fish.
3. Scenario 2 (AS2): consumption of 450 g fish/ per week, assuming the total recommended weekly fish intake from the Norwegian Directorate of Health (2011) is fulfilled by consumption of the five species in the study.

In the current risk-benefit assessment, the positive health impacts of fish consumption are compared to the adverse health effects of consumption of the five species. Hereby, benefit is defined as a decreased likelihood of adverse health effects associated with eating the fish or ingesting fish-related substances like nutrients. Whereas risk is defined as an increased likelihood of adverse health effects associated with fish consumption or ingesting fish-related substances like contaminants (Norwegian Scientific Committee for Food and Environment et al., 2022, p. p. 856).

2.6. Calculations related to potential risks and benefits

2.6.1. Selenium:Methylmercury ratio (Se:Hg) and Health Benefit Value of Selenium (HBV_{Se})

Previous studies have shown that approximately 90% of the total mercury (Hg) present in seafood occurs in the form of methylmercury (MeHg) (Afonso et al., 2019; Barone et al., 2021; EC, 2006). Based on this and the risk-benefit comparison approach of the Food and Agricultural Organization of the United Nations and World Health Organization (FAO/WHO, 2011) on fish, TWI calculations were based on the total content of Hg assuming 100% of Hg to be in the form of MeHg, to be certain of not exceeding the TWI of MeHg.

The molar ratio (Se:Hg in μmol/ g) was computed by dividing the concentrations of Selenium (Se) and Hg by their corresponding molecular weights, being 78.96 for Se and 200.59 for Hg (Barone et al., 2021; Ralston et al., 2016). Moreover, the HBV_{Se} was calculated by applying the established equation of Ralston et al. (2016) as shown in Eq. (1):

$$HBV_{Se} = \left(\frac{[Se - Hg]}{Se}\right) \times (Se + Hg) \tag{1}$$

The HBV_{Se} demonstrates whether consuming the fish will elevate (positive values) or degrade (negative values) the existing Se level. Moreover, it depends on how high the HBV_{Se} is, as this reflects the relative Se surplus or deficit brought about by consuming the fish (Ralston et al., 2016). The HBV_{Se} helps understanding the net benefit of Se coming with consumption of foodstuffs that also contain Hg, and that, moreover, possibly mitigate the toxic impact of MeHg in the body (Farina et al., 2011).

2.6.2. Health-benefit vs. health-risk related factors

In the Joint FAO/ WHO Expert Committee report about the risks and benefits of fish consumption, a framework for assessing the net health benefits/ risks of fish consumption was established, and in context, health-benefit vs. health-risk calculations were determined (FAO/WHO, 2011). Following the guidance of the FAO/ WHO, the data this RBA refers to, was used to assess the deaths prevented per million people (Eq. (2)) due to sufficient EPA+DHA intake, cancer deaths caused per million people (Eq. (3)) due to dioxin/DL-PCB intake as well as the IQ gain (Eq. (4)) and IQ loss (Eq. (5)), due to elevated intake of MeHg vs. the intake of DHA, effecting the neurodevelopment of infants. AS1 (250 g) and AS2 (450 g) were considered in the calculations.

$$\frac{Deaths \quad prevented}{million \quad people} = \frac{[EPA + DHA] \times 100 \times \frac{x}{7}}{250} \times 0.36 \times D \tag{2}$$

Where;.

- [EPA + DHA] is the total concentration of EPA plus DHA in fish (mg/ g); applies also to Eq. (3)
- 100 is the estimated fish serving size (g); applies also to Eqs. (2)–(5)
- x is the number of servings of fish per week (7 days); applies also to Eqs. (2)–(5)
- 0.36 is the proportional reduction in coronary heart disease deaths, with reduction in deaths assumed to be linearly related to DHA intake up to 250 mg/ day;
- D is the estimated number of coronary heart disease deaths per million people (1580 deaths per year per million people, calculated over 70 years).

$$\frac{Cancer \quad deaths \quad caused}{million \quad people} = \frac{[Dioxins] \times 100 \times \frac{x}{7}}{60} \times 1 \times 10^{-3} \times 10^{6} \tag{3}$$

Where;.

- [Dioxins] is the concentration of dioxins in fish (pg TEQ/ g); toxic equivalence (TEQ). The TEQ is calculated by multiplying the actual concentration with the toxic equivalence factor (TEF) of 3 * 10^{-5} as previously proposed by the World Health Organization (WHO) and reviewed by Van den Berg et al. (2006).
- 60 is the estimated body weight (kg) of a female person

$$IQ \quad points \quad gained = [EPA + DHA] \times 100 \times X \times \frac{x}{7} \times 0.04 \tag{4}$$

Where;.

- X: FAO/WHO (2011) used 0.67 as a factor to estimate the DHA concentration from [EPA + DHA]; here, specific factors were calculated for each fish species relatively, being 0.64 (Flounder), 0.50 (Lemon sole), 0.79 (Megrim), 0.90 (Thornback ray), 0.66 (Plaice)
- x is the number of servings of fish per week
- 0.04 is the coefficient relating IQ points gained to milligrams of DHA intake per day.

$$IQ \quad points \quad lossed = \frac{[MeHg] \times 100 \times \frac{x}{7}}{60} \times 9.3 \times (-0.18 or - 0.7) \tag{5}$$

Where;.

- [MeHg] is the concentration of methylmercury in fish (μg/ g); calculations were based on the total content of Hg assuming 100% of Hg to be in the form of MeHg
- 60 is the estimated maternal body weight (kg);
- 9.3 is the correlation between maternal MeHg intake and maternal hair mercury level;
- 0.18 is the central estimate of IQ points gained per microgram per gram hair mercury gained; and − 0.7 is the upper-bound estimate of IQ points gained per microgram per gram hair mercury gained. In the RBA, the upper-bound estimate of− 0.7 was applied in the calculations.

2.6.3. Fatty acids content

Eq. (6) was used to re-calculate the weight% of fatty acid methyl esters (FAME) of the studied species to obtain values in g FA/ g fillet wet weight (ww). Weihrauch et al. (1977) has previously conducted detailed research on establishing lipid conversion factors in different fish species, given as fatty acid conversion factor (FACF) in Eq. (7).

$$\frac{g \quad fatty \quad acid}{100g \quad fillet} = weight\%FAME \times FACF \times TLC \tag{6}$$

Where;.

- %FAME: results obtained from FAME analysis, presuming the same as weight%-FA since marine lipids primarily entail PUFA. The results from the established FAME procedure (Lerfall et al., 2016; Metcalfe et al., 1966) carried out by Kendler, Thornes, et al. (2023) and Kendler et al. (2023) were used as basis for calculation.
- FACF: fatty acid conversion factor expressed in g FA/ g lipid, applying the FACF (Saavedra et al., 2017; Weihrauch et al., 1977) and shown in Eq. 7.

$$FACF = \frac{0.933 - 0.143}{TLC} \tag{7}$$

Where;.

- TLC: total lipid content in g lipid/ g fillet ww (Kendler et al., 2023; Kendler et al., 2023)

2.7. Characterization of nutrients and contaminants

To define the intake of nutrients and contaminants, dietary values and health-based guidance values are employed in this study. These values are the average requirement (AR), upper limit (UL) or adequate intake (AI) for nutrients and tolerable weekly intake (TWI) for contaminants, as previously employed by the Norwegian Scientific Committee for Food and Environment et al. (2022) in a comprehensive report on fish consumption. Hereby, the scientific opinions from the European Food Safety Authority (EFSA) on specific intake values are considered for calculations of identified risks and benefits.

2.8. Statistics

For statistical analyses, the software IBM SPSS (release 28, IBM Corporation, USA) was applied. Analysis of variance (ANOVA) was carried out between the five different species, and when significant difference detected ($p < 0.05$), a Tukey HSD post hoc test was performed to investigate the differences between groups. An α-level of 0.05 was used.

3. Results

3.1. RBA assessment: BRAFO-tiered approach

3.1.1. Individual assessment of risks and benefits (Tier 1): Identification of positive health effects and hazards

Previous RBAs focusing on seafood intake identified eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), methylmercury (MeHg) as well as dioxins and dioxin-like polychlorinated bisphenyls (PCBs) as main benefit-risk components as reviewed by Thomsen et al. (2021). Based on this and the previously obtained results by Kendler et al. (2023) and Kendler et al. (2023) on contaminant levels and nutritional composition of the five fish species of interest, the following risks and benefits, as illustrated in Fig. 1, were identified for the five species.

More precisely, the concentrations of relevant components were used as a basis to assess the benefits and risks that come along with the consumption of the five fish and can be seen given per 250 g (AS1) and 450 g (AS2) in Table 2. For this, health-benefit-related calculations were executed and used as a basis for the assessment. Table 1 shows the chosen beneficial and hazardous components for this RBA, including their potential positive or negative health effects as well as suggested intakes.

3.1.2. Qualitative integration of risks and benefits (Tier 2)

The two alternative intake scenarios were opposed to the RS of zero intake and health-benefit/-risk-related factors were considered for the assessment, as previously established by FAO/WHO (2011) and Ralston et al. (2016) and can be seen in Table 2. Moreover, Table 2 shows the increase of EPA+DHA from AS1 to AS2. In AS1, the EPA+DHA contribution of the individual species ranged from 23.0% (Lemon sole) to 38.8% (Flounder) of the total RWI of EPA+DHA. Since the RS is at zero intake of the fish, health-benefit/-risk calculations on the RS are not compelling and not included in the tables. Moreover, it should be mentioned that all fish contain other LC-PUFA such as docosapentaenoic acid (DPA), being not included in RWI calculations, as no RWI suggestions are available up to date.

The increased intake of EPA+DHA and its effect on neurodevelopment in unborn infants (due to intake of the mother) is expressed as IQ points gained in Table 3 and opposed to IQ points lost due to MeHg intake. The net IQ points gained could be significantly increased from AS1 to AS2, being on average two points higher in AS2. The most significant effect on net IQ points gained was observed in megrim,

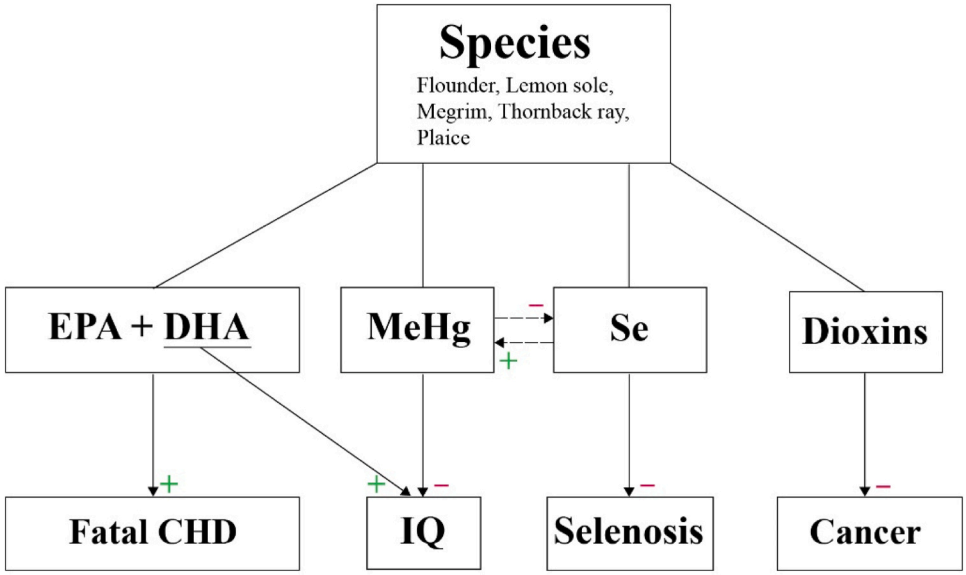

Fig. 1. Identified beneficial and hazardous components in the fish species of interest, as well as their respective health effects (+ signalling positive effects; - signalling adverse health effects); eicosapentaenoic acid (EPA); docosahexaenoic acid (DHA); methylmercury (MeHg); selenium (Se); coronary heart disease (CHD); intelligence quotient (IQ).

Table 2
concentrations of EPA+DHA (mg/ AS1; mg/ AS2) including average% of recommended weekly intake (RWI); concentrations for DPA (mg/ AS1; mg/ AS2); concentrations of Se (µg/ AS1; µg/ AS2) and% of TWI; concentrations of MeHg (µg/ AS1; µg/ AS2) as well as% of tolerable weekly intake (TWI) shown for the fillets of flounder, lemon sole, megrim, thornback ray and plaice.

Compound	Flounder	Lemon sole	Megrim	Thornback ray	Plaice	p-value[1]
EPA+DHA						
mg/ 250 g (AS1)	679.6 ± 56.8^{a}	403.3 ± 45.0^{c}	606.4 ± 30.2$^{a, b}$	569.7 ± 13.1^{b}	424.5 ± 56.4^{c}	< 0.001
% of RWI	38.8 ± 3.3	23.0 ± 2.6	34.7 ± 1.7	32.6 ± 0.8	24.3 ± 3.2	
mg/ 450 g (AS2)	1223.2 ± 102.3^{a}	725.9 ± 81.^{c}	1091.5 ± 54.4$^{a, b}$	1025.5 ± 23.6^{b}	764.2 ± 101.5^{c}	< 0.001
% of RWI	69.9 ± 5.8	41.5 ± 4.6	62.4 ± 3.1	58.6 ± 1.3	43.7 ± 5.8	
DPA						
mg/ 250 g (AS1)	38.37 ± 7.6	33.85 ± 45.0	44.49 ± 5.1	44.21 ± 14.7	66.47 ± 108.5	p = 0.942
mg/ 450 g (AS2)	69.06 ± 13.7	60.93 ± 81.0	80.08 ± 9.2	79.57 ± 108.5	119.6 ± 195.3	
Se						
µg/ 250 g (AS1)	88.41 ± 4.1$^{a, b}$	121.45 ± 1.7^{a}	99.61 ± 4.7$^{a, b}$	64.98 ± 0.3^{b}	99.99 ± 29.2^{a}	< 0.009
% of RWI	18.0 ± 0.8	24.8 ± 0.4	20.3 ± 1.0	13.3 ± 0.1	20.4 ± 6.0	
µg/ 450 g (AS2)	159.14 ± 7.3$^{a, b}$	218.61 ± 3.1^{a}	179.30 ± 8.5$^{a, b}$	116.96 ± 0.6^{b}	179.99 ± 52.6^{b}	< 0.009
% of RWI	32.5 ± 1.5	44.6 ± 0.6	36.6 ± 1.7	23.9 ± 0.1	36.7 ± 10.7	
MeHg*						
µg/ 250 g (AS1)	9.43 ± 0.4	14.5 ± 0.6	17.7 ± 2.7	43.6 ± 42.3	28.24 ± 13.5	0.178
% of TWI	12.7 ± <0.01	18.6 ± <0.01	22.7 ± <0.01	55.9 ± 0.05	36.2 ± 0.02	
µg/ 450 g (AS2)	17.9 ± 0.8	26.1 ± 1.0	31.8 ± 4.8	78.5 ± 76.1	50.83 ± 24.3	0.178
% of TWI	22.9 ± <0.01	33.5 ± <0.01	40.8 ± 0.01	100.6 ± 0.10	65.2 ± 0.03	

*MeHg is expressed as Hg, calculations made by presuming 100% of Hg is MeHg
RWI's were calculated as AI x 7
[1] ANOVA was applied to detect differences in EPA+DHA, EPA, Se and MeHg concentrations between species respectively; where significant difference was detected ($\alpha < 0.05$), a Tukey post hoc test was applied. Values with different superscript letters within a row are significantly different ($p < 0.05$)

increasing from 2.45 in AS1 to 4.41 in AS2The EFSA Scientific Panel on Contaminants in the Food Chain (CONTAM) sets a TWI of MeHg of 1.3 µg/kg body weight (b.w.) (EFSA, 2012a). Considering this suggested TWI, values respective to the alternative intake scenarios, for a person with 60 kg b.w. were calculated (Table 2). Moreover, AI's for Se intake of 70 µg/day was applied, as suggested by the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) and thereof TWI's (AI x 7) were computed (EFSA, 2014). The TWI of MeHg is not exceeded in AS1, showing acceptable values for flounder, lemon sole, megrim and plaice. In contrast, a 250 g fillet of thornback ray contributes to approximately 55.9% of the suggested TWI of MeHg. Considering the intake increase in AS2, values of thornback ray exceed the TWI (100.6%) but are within the TWI for the four other fish.

The Se:Hg molar ratio and HBV_{Se} can be used to assess whether the available Se concentration exceeds the Hg concentration and if Se moderates and even counteracts the toxicity of Hg (hence MeHg) (Barone et al., 2021). Fig. 2 visualizes the molar ratio of Se:Hg as well as the HBV_{Se} of the five fish of interest. The highest HBV_{Se} was computed for lemon sole, and showed the second highest Se:Hg after flounder. In addition, positive HBV_{Se} were calculated for all five species and the net Se concentration predominates in all species. However, no significant difference ($p = 0.167$) of the HBV_{Se} between the five species was found. All five fish show positive Se:Hg, indicating a surplus of Se over Hg. Significant differences ($p < 0.001$) were found between the five species, with flounder and lemon sole, showing significantly higher values compared to megrim, thornback ray and plaice.

The collected data on 12 different PCB and dioxin-like (DL-) PCB congeners in the studies of Kendler et al. (2023) and Kendler et al.

Table 1
Identified beneficial and hazardous components, their health effect and suggested intake.

Component	Health effect	Suggested intake/ calculation
EPA+DHA	Health-benefiting effects of LC-PUFAs: IQ point gain Decreased mortality caused by cancer and CVD	RWI[1] of 1.75 g (250 mg per day) as proposed by EFSA (2012b)
Selenium	Antagonistic effect to methylmercury; important trace element	RWI of 490 μg (based on AI x 7); UL of 255 μg/ day are considered (EFSA, 2014; EFSA Panel on Nutrition et al., 2023) HBV_{Se} and molar ratio Se:Hg
Methylmercury	Adverse-health effects of MeHg: IQ point loss due to neurotoxicity	TWI of 1.3 μg/ kg body weight (EFSA, 2012a) Molar ratio Se:Hg
Dioxins+DL-PCBs	Adverse-health effects of dioxins + DL-PCBs Increased mortality	TEQ of specific congeners

[1] Abbreviations: recommended weekly intake (RWI); tolerable weekly intake (TWI); cardiovascular diseases (CVD); health benefit value of selenium (HBV_{Se}); toxic equivalent (TEQ); intelligence quotient (IQ)

(2023) is insufficient to be included in an RBA, with only determining DL-PCB 118. DL-PCBs and dioxins are causing main health issues in humans, when compared to non-dioxin like PCBs. DL-PCB 118 was detected in European plaice in the study of Kendler et al. (2023) but below the LOD in the other four species (Kendler et al., 2023), making further calculations not feasible for all five species. Therefore, the cancer deaths caused per million people were only computed for European plaice, considering the TEQ of DL-PCB 118 for the calculation. The results given in Table 4 visualize that an increasing intake of EPA+DHA in AS1 and AS2 leads to net prevention of deaths. The concentration of PCB-118 in plaice was relatively low, showing a minor impact on mortality, which can also be expected for the four other species due to values below LOD. Nevertheless, it must be mentioned, that other dioxins or DL-PCBs might be present in the five fish species, which were not considered in the previous studies conducted by Kendler et al. (2023) and Kendler et al. (2023). Hence, values on mortality must be regarded with caution, showing rather a trend than an absolute directive.

3.1.3. *Deterministic computation of common health metric (Tier 3)*

The health-benefit vs. health-risk calculations in Tables 2, 3 and 4 indicate that the net benefits from both alternative scenarios predominate compared to the net risks, considering the mortality and child IQ point gain as indicators for assessing the public and women of childbearing age in Norway. Furthermore, the HBV_{Se} and Se:Hg ratio show a surplus of Se as shown in Fig. 2, possibly alleviating the adverse effects of an increased MeHg intake due to an increase in AS1 and AS2. Results in the current study revealed that the net benefits of increasing the intake of all five fish species are higher than the net risks for the general population and women of childbearing age with regards to IQ calculations of children. Both alternative scenarios can be considered safe, with AS2 significantly improving the intake of EPA+DHA, contributing up to 69.9% to the RWI of LC-PUFAs. Considering the estimated health benefiting and adverse factors, the assessment can be stopped at Tier 2, making further computations in Tier 3 and 4 obsolete.

4. Discussion

The present study evaluated the risks and benefits of increasing the consumption of five underutilized demersal fish species in Norway using the BRAFO-tiered approach. Moreover, RBAs carried out by the Norwegian Scientific Committee for Food and Environment highlight the importance of a sufficient intake of fish for providing essential nutrients as EPA and DHA for the Norwegian population (Norwegian Scientific Committee for Food and Environment, 2014). The previous study of Kendler et al. (2023) on the nutritional profile of the five fish species investigated in the present RBA pointed out the beneficial nutritional composition of those species, describing them as important suppliers of LC-PUFAs. Afonso et al. (2013) reports that already one portion (160 g) of megrim (*Lepidorhombus whiffiagonis*) contributes significantly to reach the EPA+DHA recommendations, coming along with low risks due to minimal concentrations of toxic trace elements. Moreover, the present RBA identified that, although all five species are considered lean fish with low fat contents in the range of 0.75–1.55% (Kendler et al., 2023; Kendler, Tsoukalas, et al., 2023), their fatty acid composition should not be underestimated, as they significantly contribute to the daily requirements set by the European Food Safety Authority (EFSA, 2012b). We estimated that the increase of portion size from 250 g (AS1) to 450 g (AS2) would lead to an average < 20% increase of n3 (omega-3)

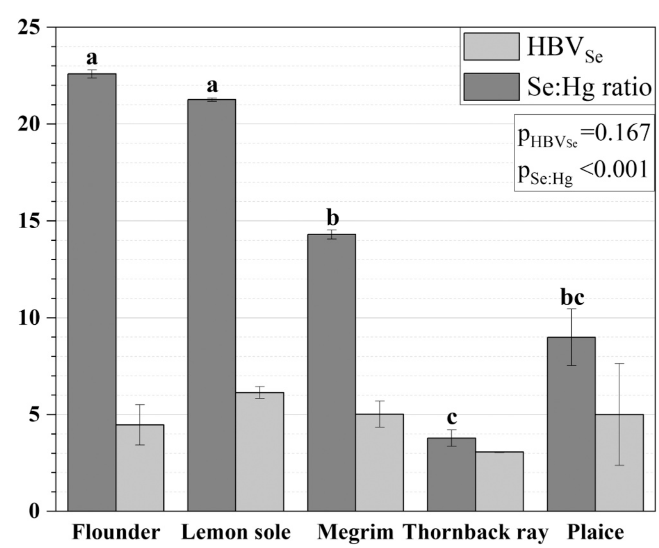

Fig. 2. Molar ratio of Se:Hg and Health Benefit Value (HBV_{Se}) of Se for the five species of interest. Error bars show SD. ANOVA was applied on species and HBV_{Se} and species and Se:Hg; where significant difference was detected ($\alpha < 0.05$), a Tukey HSD post hoc test was applied. Values with different letters (a, b) are significantly different ($p < 0.05$).

Table 3
Change of IQ Points in infants calculated from EPA+DHA intake vs. Methylmercury intake; Calculations made for the intake of for AS1 (250 g intake) and AS2 (450 g intake).

			EPA + DHA vs. Methylmercury				
			Flounder	Lemon sole	Megrim	Thornback ray	Plaice
Change of IQ Points	250 g (AS1)	IQ points gain (+)	+ 2.50	+ 1.14	+ 2.73	+ 2.93	+ 1.61
		IQ points loss (–)	– 0.15	– 0.22	– 0.27	– 0.68	– 0.22
		Net IQ gain	+ 2.34	+ 0.92	+ 2.45	+ 2.26	+ 1.38
	450 g (AS2)	IQ points gain (+)	+ 4.49	+ 2.06	+ 4.91	+ 5.28	+ 2.90
		IQ points loss (–)	– 0.28	– 0.40	– 0.49	– 1.22	– 0.79
		Net IQ gain	+ 4.22	+ 1.65	+ 4.41	+ 4.07	+ 2.11

Table 4
Change of mortality (deaths/million people) calculated from DL-PCB 118 intake. Calculations made for the intake for AS1 (250 g intake) and AS2 (450 g intake).

			EPA + DHA vs. Dioxins (PCB-118)*				
			Flounder	Lemon sole	Megrim	Thornback ray	Plaice
Change of mortality	250 g	Prevented deaths (+)	+ 15461	+ 9176	+ 13797	+ 12963	+ 9659
	(AS1)	Caused deaths (–)	/	/	/	/	– 1.8
		Net prevented deaths	/	/	/	/	9657
	450 g	Prevented deaths (+)	+ 27830	+ 16517	+ 24835	+ 23333	+ 17386
	(AS2)	Caused deaths (–)	/	/	/	/	– 3.3
		Net prevented deaths	/	/	/	/	17383

*values of PCB-118 are below the limit of detection (LOD) and hence not included in this RBA (Kendler et al., 2023).

long-chain polyunsaturated fatty acids. For example, when comparing these two scenarios for flounder, an increase in the contribution of EPA+DHA from 38.8% to 69.9% was identified. Nevertheless, AS2 is not sufficient in providing 100% of the daily required EPA+DHA concentrations, which is why substituting the intake of fatty fish with 250 g of any of the five investigated lean fish as suggested in AS1 should be considered. In spite of the lack of an RWI for DPA, research indicates that the evidence on health benefiting characteristics of DPA is increasing (Calder, 2014). DPA is the intermediate product of EPA and DHA, and is suggested to mediate similar functions in human metabolic processes (Kaur et al., 2011). This contributes to the health benefits of an increased intake of the five species through LC-PUFAs.

The MeHg values for the four flatfish species were found to be considerably below the TWI. However, when consuming thornback ray, higher exposure to MeHg must be considered in intake suggestions, with AS1 contributing to 55.9% and AS2 exceeding the TWI (100.6%) of MeHg. Elasmobranchs, such as thornback ray, are potentially more exposed to accumulation of pollutants and toxic trace elements due to their higher trophic level in the food chain as well as general slow reproductivity and maturity, similar to large mammals (Tiktak et al., 2020). However, health-benefiting properties can be linked to the consumption of all fish species with regards to Se. The present study estimated that the five fish's Se concentrations contribute on average with 20% to the RWI in AS1 and up to 44.6% in AS2. The upper limit for Se for adult people of 255 μg/day (EFSA Panel on Nutrition et al., 2023) was not exceeded in any scenario for any species. The beneficial Se concentrations can be opposed to the concentrations of toxic MeHg. The Se:Hg as well as HBV_{Se} were considered for the five fish species (Fig. 2). Se:Hg exceeding 1 indicate a protective effect of Se against the toxicity of Hg (Peterson et al., 2009). All five investigated fish have higher total Se concentrations than Hg, hence exceed a molar ratio of 1, with flounder showing the highest (Se:Hg > 22). Moreover, HBV_{Se}'s of three to six were found in the current study, indicating a surplus of Se and preventive effects opposing the MeHg exposure. In a comparable RBA considering Hg, MeHg and Se concentrations in elasmobranch meat, thornback ray showed the highest HBV_{Se} compared to other rays, skates and sharks with a value of about 6 (Storelli et al., 2022). This is in accordance to a positive HBV_{Se} found in the present study and indicates a positive antagonistic effect of Se on the MeHg toxicity. Azad et al. (2019) found a molar ratio (Se:Hg) of 23.2 and HBV_{Se} of 4.76 for plaice in a study from the Northeast Atlantic. Barone et al. (2021) found Se:Hg's of approximately three to four for three different rays as well as for turbot and Common sole. Moreover, HBV_{Se}'s of around 2–6.5 were found by Barone et al. (2021). In addition, child IQ gain/ loss as the common health metrics considering MeHg and EPA+DHA intake was considered. The MeHg intake showed almost no influence on IQ points due to low concentrations in all five fish species, suggesting low exposure when consuming these species. Moreover, a net gain in IQ points was identified in both AS1 and AS2 for all fish, due to a satisfying intake of EPA+DHA.

The European Commission (EC) has set maximum levels of 6.5 ng TEQ/ kg muscle meat of fish and fishery products to address the risks of unwanted intake of dioxins and DL-PCBs (EC, 2011). Frantzen et al. (2020) assessed multiple dioxins and DL-PCBs for European plaice in 54 pooled samples, containing 448 individuals and got an average concentration of 0.52 and median of 0.50 ng TEQ/ kg fillet ww of for all samples. Both the obtained values in the comprehensive report of Frantzen et al. (2020) and the values used in this RBA are significantly lower than the recommended values of the EC. Moreover, calculations on the mortality due to PCB and dioxin intake vs. EPA+DHA intake concluded a net prevention of death when consuming plaice, promoting the overall low values of contaminants. It can be suggested that an increased consumption of plaice as suggested in AS1 and AS2 can be regarded as safe with respect to the relative dioxin and DL-PCB concentrations. Furthermore, it can be argued that the consumption of the four other fish species can be assumed as safe, as they inhabit the same environments as European plaice, making a proximate evaluation of their expected contaminant concentrations and health effects possible. Due to a high lipophilicity PCBs and DL-PCBs tend to accumulate in the adipose tissue of fish (Zhang et al., 2012), whereas Hg and MeHg are supposed to accumulate in the muscle tissue, due to closely binding to thiol groups in (seleno)proteins (Bosch et al., 2016). The five fish species in the present study are regarded lean fish with fat contents below 2%, which speaks against the general likelihood of elevations of PCBs or dl-PCBs (Kendler, Thornes, et al., 2023; Kendler, Tsoukalas, et al., 2023). Zhang et al. (2012) reported higher PCB accumulation in tails, compared to dorsal and ventral muscle samples. In addition, Barbosa et al. (2018) found differences of toxic element accumulation between different muscle parts, reporting higher accumulation of Hg (among others) in the central muscle compared to edge parts of megrim (*Lepidorhombus whiffiagonis*), but being within the defined acceptable limit of 1 mg/ kg for *Lepidorhombus* species (EC, 2006). This is in accordance with results obtained for megrim (0.071 mg/ kg or 17.7 μg/ 250 g) in the present study.

The BRAFO-tiered approach is a well-established method to assess risks and benefits of foods and has been followed in multiple assessments (e.g. Gao et al. (2015); Hoekstra et al. (2013); Schütte et al. (2012); Watzl et al. (2012)). A RBA study on the consumption of marine species in the Chinese population carried out by Gao et al. (2015) applied similar health metrics established by FAO/WHO (2011), as the present study. The qualitative RBA of Gao et al. (2015) lead to similar results, where the alternative scenario led to clear net beneficial effects on the prevention of deaths and child IQ gain outweighed the exposure of dioxins and MeHg for fish consumed in China. In addition, the results in the present RBA stress that the BRAFO-tiered approach is a useful methodology to clearly weigh out risks and benefits of marine fish.

It is important to note that there were some limitations in our RBA study, including a fragmentary screening of toxins, excluding major toxic dioxins as well as the limited availability of consumer intake data which only allowed for a qualitative RBA approach. To conduct a quantitative RBA, a comprehensive data set including sufficient information on intake frequency and amount of the investigated species is required. Quantitative RBAs on fish as carried out by Carvalho et al. (2022) can give comprehensive information on the prevention of DALYs due to sufficient and regular fish intake, especially important for policy makers and authorities. Nevertheless, a qualitative RBA, such as carried out in this study, generates important knowledge, and gives information to relevant policy makers and authorities in Norway. Our RBA created valuable knowledge for five species that have so far not been of large commercial interest in Norway. This is the first RBA carried out on these five fish species in the country, and it can be used as a directive for safe consumption of these underutilized fish species.

5. Conclusions

The present study not only emphasized the beneficial outcomes of consuming the five investigated underutilized fish species, but also highlighted that these benefits outweigh potential risks. Consequently, the findings strongly support an increased intake of these five species originating from Norway for the Norwegian population, effectively highlighting their positive health benefits. An optimal weekly fish intake of 300–450 g of which 200 g should be fatty fish can be regarded as feasible intake scenario. The substitution of 250 g of any of the five investigated lean fish should be preferred, as suggested in AS1. To get information on DALY and QALY connected to the consumption of the five studied fish, more data on the population is required, which can be done in future works in this field. Even though not all possible contaminants (e.g. multiple dioxin, DL-PCB congeners) were considered in this study, our results support a recommendation for increasing the consumption of these five species. We believe that this RBA can help promote the consumption and commercialization of flatfish and rays in the Norwegian market.

CRediT authorship contribution statement

Sophie Kendler: Conceptualization, Methodology, Investigation, Writing – original draft. **Sara Monteiro Pires**: Validation, Methodology, Writing – review & editing. **Anita Nordeng Jakobsen**: Conceptualization, Supervision, Validation, Writing – review & editing, Funding acquisition. **Jørgen Lerfall**: Conceptualization, Supervision, Validation, Writing – review & editing, Project administration, Resources, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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