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Methylmercury contamination in Mediterranean seafood: Exposure assessment and cost of illness implications

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HIGHLIGHTS

- First transdisciplinary assessment of MeHg impacts in the Mediterranean, linking seafood contamination and illness costs.
- Granular data and dietary surveys estimate seafood consumption across Mediterranean countries.
- Mediterranean seafood consumption may cause MeHg exposure, affecting children's neurodevelopment.
- Annual health costs from MeHg in Mediterranean seafood exceed €10 billion.
- New methodology to estimate MeHg exposure levels from seafood consumption.

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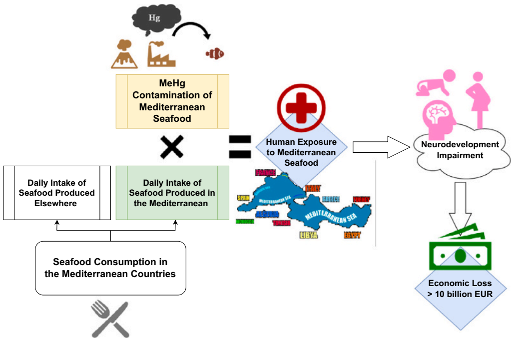
GRAPHICAL ABSTRACT



ABSTRACT

Methylmercury (MeHg) is a widespread contaminant that bioaccumulates in marine food webs, including those in the Mediterranean sea. It poses serious health risks, especially to developing infants and children, where exposure can cause neurological damage and developmental delays. In addition to health concerns, high MeHg

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levels in seafood can lead to economic losses through cognitive impairments that reduce productivity. Despite seafood being a dietary staple in Mediterranean countries, the full extent of MeHg's health and economic impacts remains underexplored, especially with the rising international trade.

This study aims to (a) estimate MeHg exposures in Mediterranean populations from consumption of Mediterranean seafood and (b) quantify the economic costs associated with MeHg intake. We assessed population exposures in Mediterranean countries by combining a highly granular seafood supply data on Aquatic Resource Trade in Species (ARTIS), alongside Global Dietary Database (GDD) and review of MeHg levels in Mediterranean seafood. The economic cost was then derived by linking MeHg intake to productivity losses associated with cognitive deficits. As a result, we estimate that Mediterranean countries experience over €10 billion in annual economic losses due to IQ-related productivity decline associated with MeHg exposure from consuming seafood sourced from various fishing areas of the Mediterranean Sea. The novelty of this research lies in its transdisciplinary approach to MeHg impact assessment that incorporates highly detailed seafood supply data with dietary surveys, and scientific literature to provide a more realistic and detailed view of MeHg exposures and the associated cost-of-illness from local seafood consumption accross Mediterranean countries. These findings highlight a critical aspect of MeHg management: while international trade can mitigate local exposure by providing access to less-contaminated imports, it simultaneously exports the contamination burden to other regions. This duality emphasizes the importance of global cooperation in addressing seafood safety and managing transboundary MeHg risks.

1. Introduction

The Mediterranean Sea is viewed as an ecosystem especially vulnerable to pollution owing to a multitude of contributing factors. It is a semi-enclosed basin with a slow renewal time averaging 50 to 100 years (Millot and Taupier-Letage, 2005). Surrounded by the continental areas of Southern Europe, Northern Africa and the Middle East, the Mediterranean basin faces significant pressure from many important anthropogenic activities, including extensive industrial operations, massive tourism, major maritime transport routes, and densely populated coasts, etc. (UNEP/MAP and Plan Bleu, 2020). Despite substantial efforts made to manage and mitigate pollution under international agreements such as the Barcelona Convention and its associated protocols, the Mediterranean Sea remains one of the most heavily polluted seas in the world (MedECC, 2020). Among the contaminants of greatest concern for human health, there is mercury (Hg), a toxic heavy metal, and its methylated form, methylmercury (MeHg), found in marine environment (Landrigan et al., 2020).

Mercury pollution in the Mediterranean Sea stems from a combination of both legacy pollution and ongoing emissions from industrial activities, including mining, coal combustion, waste incineration, land and maritime shipping and other sources (Weiss-Penzias et al., 2013). The United Nations Environment Program has estimated that 20,000 tons of mercury still end up in the environment annually (UN Environment, 2019). Once released, Hg can be transported over long distances and eventually deposited into the Mediterranean Sea through atmospheric deposition and river runoff (Cossa et al., 2022). In the sea, a large part of Hg is transformed into MeHg (Lehnherr et al., 2011; Monperrus et al., 2007) which bioaccumulates in marine organisms moving up the food chain and becoming extremely concentrated in higher trophic level fish such as tunas, a process also known as bio amplification (Storelli et al., 2010). The Mediterranean sea has one of the highest Hg methylation potentials worldwide. Microorganisms such as Nitrospina play likely a key role in methylation in Mediterranean waters (Villar et al., 2020), since this region is characterized by high levels of methylmercury in some basins, attributed to specific microbiological activity and low water turnover conditions, favoring bioaccumulation in marine trophic chains. Mediterranean bluefin tunas show the highest MeHg accumulation rates compared to fish caught in other parts of the world (Cossa et al., 2022). Marine fish consumption is considered the main route of MeHg exposure to humans and Mediterranean populations might be particularly vulnerable to dietary MeHg exposure since seafood is central to their diet (Lloret, 2010). This poses serious human health threats stressing the importance of assessing MeHg exposure and the resulting Cost-of-Illness in the region.

Being a very potent neurotoxic compound, MeHg is able to alter the nervous system in infants and children (Grandjean et al., 2010). By causing irreversible alterations in the structure and function of the developing nervous system, MeHg leads to significant deficits in cognitive thinking, memory, attention, language, fine motor skills, and visual-spatial skills (Cohen et al., 2005). MeHg exposure has also been linked to cardiovascular diseases and nervous system damage in adults (Landrigan et al., 2020). In addition to these public health concerns, MeHg intoxications can be a significant economic burden associated with direct, indirect and intangible costs. Direct costs include medication expenses or support services. Indirect costs are a result from decreased productivity of patients themselves or those who care for patients, as well as reduced school attendance, investments in the health system, etc. Finally, intangible costs result from the pain and suffering caused by the disease (Jo, 2014). The toxicity of MeHg raises serious concerns about seafood safety and public health, and these potential economic impacts emphasize the need for a thorough exposure and Cost-of-Illness assessment in the Mediterranean region.

The health implications of MeHg exposure and their socio-economic costs have prompted the implementation of policies and regulations to limit Hg releases from human activities and to control its transport at local, regional, and global scales (Bank, 2020). At the international level, since the 2nd Minamata Disease Research Group revealed in 1973 the chronic health effects of MeHg exposure through fish consumption, MeHg has been the subject of extensive monitoring by the scientific community and national agencies (Cinnirella et al., 2019). At the regional level, the programs associated with the Mediterranean Action Plan (MAP) of 1975 have also led to substantial monitoring efforts of Hg in the Mediterranean biota. Hence, over the last four decades, biomonitoring programs (e.g. Si.Di.Mar., MED POL, and IFREMER) conducted by seafood safety agencies and researchers in the Mediterranean Sea have provided valuable data for estimating the mercury levels in commercially important seafood species from various Mediterranean regions, (Cinnirella et al., 2019).

Exposure to MeHg can be determined either by using mathematical models along with input data (such as fish mercury levels and dietary patterns) or through biomonitoring studies that measure MeHg directly in biological samples such as blood, urine, hair, or nails (World Health Organization and Food and Agriculture Organization of the United Nations, 2009). Even though biomonitoring studies can provide valuable information about population exposure to mercury, they are limited to specific areas and can be expensive and resource intensive, making them unavailable for many countries. The latest Global Mercury Assessment Report highlighted a general lack of regional monitoring programs, and that countries with the highest fish consumption are often poorly covered by biomonitoring efforts (UN Environment, 2019). Therefore, it is necessary to develop new methods estimating habitual seafood consumption or the intake of specific nutrients and/or contaminants such as the Food Frequency Questionnaire recently developed by De Giovanni et al. (2023) to compare the results with limits set to protect human health.

Representative surveys are considered to be the gold standard in this domain with Global Dietary Database (GDD) being the largest archive of surveys from different countries and regions which serve as a basis for improving our understanding of consumption levels around the world. In most cases, however, those surveys focus on overall seafood consumption and do not provide sufficient detail into the origins of the seafood that play an essential role in determining the actual population exposures. This is especially important now more than ever, given the considerable levels of international seafood trade. However, the complexity of global value chains often obscures the origins of the products. As a result, we may be aware of local contaminations, but we no longer know where exactly our food comes from and if it is actually safe to consume.

Most often exposure assessments do not account for international trade because of the lack of data. Considering trade in exposure assessment remains, however, crucial for better understanding the flow of nutrients, contaminants, and toxins across nations. For instance, the level of contamination in different seas and oceans is not necessarily the same. Thus, it is first necessary to determine the origin of seafood to accurately estimate potential exposures. The analysis is often complicated, however, by international trade since we can no longer say that everything that was locally produced is also consumed by local populations. Recently several exposure assessments (Xing et al., 2023; Zhang et al., 2021; Zhou et al., 2024) attempt to address the gap by using FAO supply and BACI trade datasets as a preliminary way of taking trade into consideration. But a significant lack of publicly available datasets remained a major challenge up until recently. Drawing on years of research and expertise, a team of researchers bridges this gap in the ARTIS database which should enhance the accuracy of the research by providing a more detailed analysis of nutrient and contamination flows between nations (Gephart et al., 2024).

The comparison of consumption levels reported by GDD and computed by dividing ARTIS supply by the size of adult population and the number of days in a year reveals that ARTIS data being the measure of total supply may overestimate the consumption levels of population of interest. This is especially true for countries like Malta where the number of tourists who also contribute to consumption levels exceeds total population by multiple folds. Thus, when the objective is to estimate the consumption levels of local population, surveys still provide a better estimate of actual overall population consumption.

By combining data on contamination levels and consumption patterns, a more robust and flexible methodology can be established for conducting comprehensive exposure assessments.

Based on available data and research, several countries and international organizations have established reference levels for weekly MeHg intakes and the maximum allowable amount of (Me)Hg in seafood considered to be safe (or without appreciable risk to health). For example, the European Food Safety Authority (EFSA) Panel on Contaminants in the Food Chain (CONTAM) established a tolerable weekly intake (TWI) of 1.3 $\mu g \cdot [kg\ BW]^{-1} \cdot week^{-1}$ in 2012 (that is, 0.19 $\mu g \cdot [kg\ BW]^{-1} \cdot day^{-1}$). The European Union regulation 2023/915 sets a general limit of 0.5 $mg \cdot kg\ FW^{-1}$ in fishery products with several exceptions for specific species for which the threshold is 0.3 or 1.0 (European Union, 2023). In more recent development, the U.S. Agency for Toxic Substances and Disease Registry (ATSDR, Department of Health and Human Services) proposed a lower chronic Minimal Risk Level (MRL) of 0.1 $\mu g \cdot [kg\ BW]^{-1} \cdot day^{-1}$ (ATSDR, 2022) corresponding to a hair-Hg concentration of about 1 $\mu g \cdot g^{-1}$ hair (Bellanger et al., 2013; Staff et al., 2000). Updated calculations (Bellanger et al., 2013; Grandjean and Budtz-Jørgensen, 2007) resulted in another biological limit which is about 50 % below the recommended level and corresponds to 0.58 $\mu g \cdot g^{-1}$ hair. The validity of this lower cut-off point below the reference level is supported by studies of developmental neurotoxicity at exposure levels close to the background (Bellanger et al., 2013). On the international scale, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) considers MeHg in seafood products as safe when the reported concentrations do not exceed the threshold limits of 0.5 $\mu g \cdot g^{-1}$ WW and 1 $\mu g \cdot g^{-1}$ WW for fish (excluding predatory fish) and predatory fish, respectively. As to the provisional TWI, JECFA revised its recommendations for MeHg from 3.3 to 1.6 $\mu g \cdot [kg\ BW]^{-1} \cdot week^{-1}$, based on the most sensitive toxicological end-point in the most susceptible species (humans). For most adults, intakes up to two times higher than the PTWI should not pose any risk of neurotoxicity taking into account the possible compensation of MeHg toxicity by beneficial nutrients in seafood (Joint Expert Committee on Food Additives, 2004), such as n-3 polyunsaturated fatty acids and selenium. Nonetheless, MeHg intake should not exceed the PTWI for women of childbearing age in order to protect the embryo and fetus (Joint Expert Committee on Food Additives, 2004).

These observations emphasize the need to examine MeHg impact on children's neurodevelopment and the estimated associated economical cost in the Mediterranean countries. In this study, to compensate the lack of seafood consumption data in several Mediterranean countries, we propose a new methodology for estimating population exposure levels based on Global Dietary Database (GDD) and recently published dataset on Aquatic Resource Trade in Species (ARTIS) which not only harmonizes the available supply data but also accounts for the provenance (origins) of different seafood species in local consumption. Finally, we perform the first Cost-Of-Illness analysis to assess the economic burden of MeHg exposure resulting in the productivity decline of the Mediterranean region.

2. Materials and methods

2.1. Assessment of Mediterranean seafood contamination

Conducting exposure assessment requires a combination of important elements, including but not limited to reliable and comprehensive seafood contamination data that we collect based on the recent literature published on Scopus and Pubmed. Given our focus on Mediterranean seafood, we search for “mediterranean” AND “mercury” within title/abstract. The resulting articles are further filtered based on the publication period (from 2015 to 2022) and the relevance of the title/abstract. The remaining 88 articles are manually screened to exclude references that report Hg levels in sediments/humans, do not report mean estimates or do not provide sufficiently readable tables/graphs making it complicated to obtain the exact estimates. The initial dataset includes 73 papers which is equivalent to 25,152 observations. Most of the observations come from the recent publication of Cinnirella et al. (2019) which compiles 24,465 data points from biomonitoring programs conducted by seafood safety agencies and researchers between 1969 and 2015 in the Mediterranean Sea. For the analysis, the initial dataset was further refined, following established practices, as outlined in the Supplementary material, and focusing on FAO Divisions (major fishing areas) corresponding to the Western, Central and Eastern Mediterranean, specifically subarea 37.1, 37.2 and 37.3, respectively. First, we exclude references with lacking, unclear or irrelevant fishing area (as per FAO Division) information as well as Black and Marmara Seas which are not well represented in our dataset. Second, we remove inedible and rarely consumed species based on their kingdom, class, protection status or non-marine habitat with a detailed list provided in Table S3. Third, we eliminate non-edible tissues (Table S4), and we remove total Hg observations if a study reports both total Hg and MeHg levels for the same combination of species, tissue code and location (Table S5). In six cases in which a study reports several types of edible tissues for the same sample and location, we retain the most comprehensive one (Table S6). Finally, when both datasets, newly created and Cinnirella et al. (2019), report observations for the same reference, we exclude the equivalent study (reference 80 and 312) from Cinnirella et al. (2019) (Table S7). For more details, please refer to the accompanying R script and codebook provided as Supplementary Material.

The resulting dataset covers the sampling period between 1969 and 2019 in 7 FAO Divisions (from 37.1.1 to 37.3.2) and contains 17,934 observations with 17,296 of them coming from Cinnirella et al. (2019). The rest of the data points follow the same principle of data granularity (i.e., the lowest level of information) reporting mean concentrations and their standard deviations whenever they were available. For harmonization purposes, all observations were converted to the same units of measurement – $\mu g \cdot g^{-1}$. Furthermore, the same conversion factors were adopted from Cinnirella et al. (2019) to harmonize measurements of Hg in tissues with different water content (WW = wet weight; DW = dry weight). References that did not clearly specify the weight type were assumed to be WW which is more often reported in the literature. For risk assessment purposes, total Hg concentrations are converted to MeHg following the guidelines of the European Food Safety Authority (EFSA) that proposes a conversion factor of 1.0 and 0.8 for fish and molluscs/crustaceans, respectively (EFSA, 2012). Finally, as MeHg concentrations seem stable across the years (Fig. S1), the summary statistics are calculated using the entire sampling period. The common statistics, such as mean, median as well as different percentiles for each seafood category in different FAO Divisions further serve as a basis for various exposure scenarios.

2.2. *Mediterranean seafood and its consumption estimates in FAO divisions*

The second crucial element for successful exposure assessment consists in determining consumption levels per capita.

In this article, we argue that ARTIS supply data should be incorporated into the analysis because it provides important information for national seafood endowment (preferences) which can be expressed in the form of shares and applied to GDD overall seafood consumption estimates to derive the contributions of different species (groups of species), countries and FAO divisions to overall population exposures. To ensure that these shares are derived under the same conditions as the consumption data, we convert ARTIS live weight supply into edible weight using average conversion factors (as detailed in Material and method and in Supplementary Material) that we compile for various groups of seafood (FAO/INFOODS, 2016; Torry Research Station, 1989). We then assume that molluscs and crustaceans are consumed in the form of edible meat, while fish – in the form of edible flesh which comprises a slightly larger portion than skinless fillet and provides a more cautious estimate. Neither approach is perfect since we don't possess enough data for dietary habits in different countries. Nonetheless, the conversion process ensures that we compute the shares of Mediterranean sourced groups of seafood under comparable to edible conditions. We further link the local production with “FAO regional capture fisheries statistics v2024.1.1” and “FAO global fishery and aquaculture statistics v2024.1.0” allowing us to attribute Mediterranean seafood production to FAO Divisions of origin based on their relative share which is further linked to previously calculated contamination levels of FAO divisions. Finally, rfishbase package in R is used to attribute trophic levels to different species found in ARTIS dataset. When trophic levels are not available, we compute the average trophic levels for ISSCAAP Groups and attribute them to the remaining species of the corresponding groups. The graphical representation of the methodology is summarized in Fig. 1.

2.3. *Burden of disease, lost IQ and share of population shifted to mild mental retardation*

Prenatal MeHg exposure is well known to cause IQ losses and associated neurodevelopmental deficits. In its safety evaluation of MeHg in food, the World Health Organization (WHO) highlights that neurodevelopment is the most sensitive health outcome of MeHg exposure, particularly in-utero (Poulin et al., 2008). As a result, to assess potential health impacts in various populations WHO develops a methodology for estimating MeHg associated burden of disease based on the established linear no threshold dose-response relationship between each $\mu g \cdot g^{-1}$ increase in maternal hair mercury and a 0.18-point decrease in IQ (Axelrad et al., 2007; Poulin et al., 2008).

While preferring level of impregnation measures for assessing the body burden of mercury (e.g. hair, blood, cord-blood), WHO also provides a model for estimating blood mercury levels from food intake and then converting them to hair concentrations (Poulin et al., 2008). The relationship may not be an accurate indicator of population hair Hg levels due to individual variability in absorption and elimination rates (Canuel et al., 2006; Poulin et al., 2008), but it is still a useful approximation for high level assessments, especially when direct measurements are not available (Poulin et al., 2008).

The burden of disease methodology then derives percentage of population shifted to mild mental retardation (MMR) based on the assumption that intelligence in human populations approximates a normal distribution, with a mean of 100 IQ points and a standard deviation of 15 IQ points (NRC, 2000; Poulin et al., 2008). Percentage of the population exposed to MeHg was also initially assumed to follow normal distribution since the original WHO report considered only a sub-group of population with high mercury exposure where normal distribution may be expected. For our analysis, however, we slightly modify this approach by assuming log-normal MeHg distribution in accordance with the right skewed distribution of the compiled MeHg dataset. From the theoretical point of view, log-normal distribution also makes sense since MeHg observations are bounded at zero (cannot be negative) with most consumers being exposed to lower MeHg levels and very small part of the population being exposed to very high MeHg levels as empirically reflected in the available dataset. The mean and standard deviation of MeHg required for estimating the burden of disease are obtained from the literature review. The MeHg levels are first converted into natural logarithms with mean values being estimated on the logarithmic scale to reduce the impact of outliers. Fishmethods package function “bt.log” in R is then applied to these estimates to convert the results into the original scale.

2.4. *Economic costs of MeHg exposure: cost-of-illness analysis*

As documented in (Bellanger et al., 2013), the major component of social costs of IQ reduction are lost productivity and lower earning potential. Consequently, in accordance with the existing literature, the economic impact of prenatal MeHg exposure in this study is measured as total lifetime productivity (earnings) loss associated with decreased IQ levels in newly born infants. We assume a 1 % decrease in IQ to be associated with a 1.4 % drop in lifetime earnings as recommended in recent literature review (Grosse and Zhou, 2021).

Given the lack of data on lifetime productivity in Mediterranean countries, we derive the corresponding value from an updated estimate for the United States which amounted to $1,468,669 in total productivity of newly born infant in 2016, with $934,583 and $534,086 being attributed to market and non-market productivities respectively (Grosse et al., 2019). In order to eliminate price/productivity differences and to assure the applicability of these estimates to the Mediterranean countries, we proceed in accordance with recent health economics literature review (Turner et al., 2019). We first adjust this number to 2021 prices using US Implicit GDP Deflator of 1.122 as provided by Federal Reserve Economic Data (FRED) database. We then apply IQ-associated change in lifetime productivity and obtain the value of $23,070 (expressed in constant 2021 USD) per IQ point. Following (Bellanger et al., 2013), the number is further adjusted for price/productivity differences between countries using Purchasing Power Parity (PPP) conversion rate and the ratio of PPP-adjusted real GDP/capita in each country in relation to the US as a reference (as detailed in Material and method and in

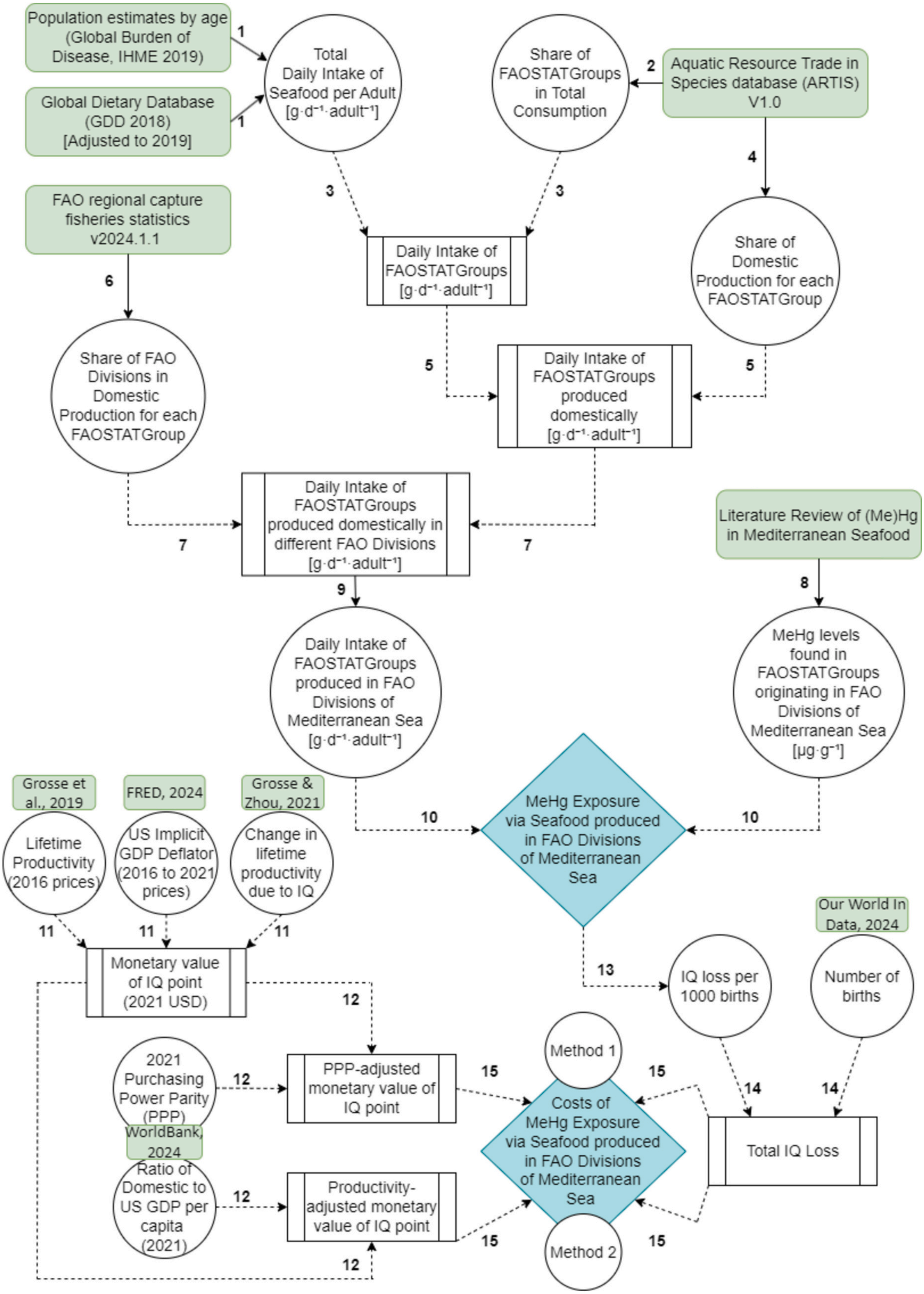

Fig. 1. Graphical representation of applied methodology.

Supplementary Material). The results are then expressed in constant 2021 EUR using exchange rates provided by the World Bank.

3. Results

3.1. Mediterranean seafood contamination

In total, this study's (Me)Hg database comprises 17,964 data points. These observations correspond to the mean MeHg values in edible tissues of 267 Mediterranean marine species and are plotted against the corresponding trophic levels (TL) in Fig. 2.

1.6 % of small pelagic marine fish, 7.62 % of molluscs, 20.8 % of small demersal marine fish, 23.7 % of large demersal marine fish, 29.4 % of cephalopods, 39.8 % of crustaceans, and 49.3 % of large pelagic marine fish were above the JECFA threshold limit of 0.5 μg · g^{-1} for non-carnivorous fish. As expected, larger species at the top of food chain more often presented MeHg levels above the upper JECFA limit of 1 μg · g^{-1} for carnivorous fish, with 12.3 % of crustaceans, 11.4 % of large demersal marine fish, and 26.2 % of large pelagic marine fish being above this limit. Finally, only 2.39 % of large demersal and 4.27 % of large pelagic marine fish presented MeHg levels above the WHO limit of 2.5 μg · g^{-1}. However, this finding once again confirms that smaller fish are to be preferred for consumption.

The mean MeHg levels found in seafood sampled from different Mediterranean regions are summarized in Table 1. The number of samples varied between FAO fishing zones and by countries. The Sardinia FAO fishing zone was the most represented and accounted for 31 % of the samples included in the database ($N = 5668$). On the contrary, the Aegean FAO fishing zone was represented in only 3.87 % of the samples ($N = 694$). By country, Italy had the most samples ($N = 7311$; > 40 % of samples). It was followed by France (15 %), Israel (13.6) and Spain (12.7 %). There was little data for Southern and Eastern Mediterranean countries but combining sampling efforts from various countries by FAO Divisions with the information on capture provenance still allows us to obtain better estimates for most seafood categories.

It is also of interest to determine the maximum weekly intake of Mediterranean seafood that is safe to consume based on threshold values set by international organizations. To achieve this, it is sufficient to divide these values by the actual contamination of different FAOSTAT groups in FAO Divisions. Several scenarios are presented in tables S1-S2 and can further be used as a reference for developing optimal seafood intake that would minimize MeHg exposures.

3.2. Seafood consumption levels in Mediterranean countries

According to the Global Dietary Database (GDD), Israel exhibits the highest seafood consumption among Mediterranean countries, followed by Spain, Italy, Montenegro, and Tunisia, as demonstrated in Fig. 3. When comparing daily seafood intake levels between the ARTIS and GDD databases, we find that the estimates for most countries align well between these two methods. However, since the ARTIS database is based on trade data, it may overestimate actual exposures, particularly in countries like Malta, where the number of tourists, who also contribute to consumption levels, far exceeds the total population. Nonetheless, incorporating ARTIS into the analysis provides a unique opportunity to gather detailed information about seafood provenance and national preferences across Mediterranean countries.

This additional layer of detail is especially important considering rising levels of international trade and high level of heterogeneity in consumption preferences among nations. Fig. 4 further illustrates the breakdown of seafood consumption across various categories—cephalopods, crustaceans, molluscs, (large/small) demersal and (large/small) pelagic marine fish as well as freshwater/diadromous fish and aquatic animals—across different Mediterranean countries.

For instance, several countries show notably high daily intake of cephalopods, with Spain and Italy having the highest values at 15.21 g · $adult^{-1}$ · day^{-1} and at 14.43 g · $adult^{-1}$ · day^{-1} respectively, followed by Slovenia, Croatia, Greece, and Cyprus. While Italy shows a marked preference for other molluscs as well with 6.73 g · $adult^{-1}$ · day^{-1} consumed daily, the crustaceans can be considered a staple food in such countries like Spain, Italy, Albania, Morocco, Israel, and France.

Furthermore, while not included in further analysis, freshwater and diadromous fish consumption also displays a large disparity, with Israel dominating this category at 88.43 g · $adult^{-1}$ · day^{-1}—much higher than any other country. Last but not least, even if fish continues to take up the largest portion of national daily seafood intake for most countries, the preferences for small and large fish vary significantly across the Mediterranean as demonstrated in Fig. 4. Therefore, it is essential to

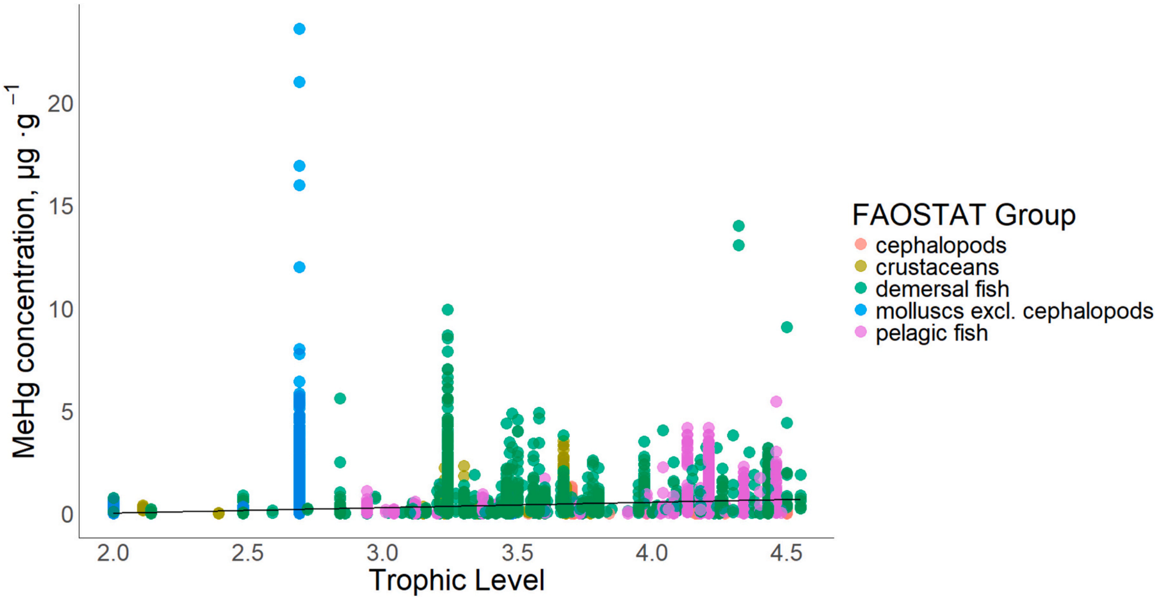

Fig. 2. Mean mercury levels (μg · g^{-1} WW) reported in Mediterranean marine species plotted against the trophic level of the species. Each data point represents the mercury levels measured in one species and from one study selected in the literature review. (Source: own compilation based on data from literature review as detailed in Section 2.1.)

Table 1
Mean MeHg levels (μg · g^{-1} WW) and associated number of samples of seafood species from different Mediterranean regions. To calculate the mean MeHg levels, the data obtained from the literature review are first converted into natural logarithms with mean values being estimated on the logarithmic scale. The fishmethods package function "bt.log" in R is then applied to these estimates to convert the results into the original scale. The number of samples (n) corresponds to the number of samples from which mean MeHg contamination levels were estimated.

FAO Groups	Balearic (37.1.1)		Gulf of Lions (37.1.2)		Sardinia (37.1.3)		Adriatic (37.2.1)		Ionian (37.2.2)		Aegean (37.3.1)		Levant (37.3.2)	
	Mean	n	Mean	n	Mean	n	Mean	n	Mean	n	Mane	n	Mean	n
Cephalopods	0.19	16	0.33	(*)	0.47	283	0.16	3	0.05	53	0.09	(**)	0.14	8
Molluscs excl. Cephalopods	0.05	866	0.02	1830	0.46	2205	0.11	1672	0.22	496	0.07	247	0.16	965
Crustaceans	0.26	423	1.06	5	0.72	849	0.19	24	0.30	44	0.24	54	0.05	42
S_DF	0.17	1025	0.21	193	0.87	1394	0.51	234	0.40	330	0.16	329	0.24	1618
S_PF	0.13	329	0.06	12	0.19	481	0.15	105	0.17	77	0.24	9	0.13	89
L_DF	1.15	35	0.59	115	0.59	184	0.24	46	1.09	56	0.12	32	0.20	242
L_PF	1.09	177	1.11	206	1.60	272	0.66	30	0.50	146	0.28	23	0.11	59
n total		2871		2361		5668		2114		1202		694		3023

(*) MeHg for cephalopods in FAO Division 37.1.2 are estimated by taking the arithmetic mean of mean MeHg values for cephalopods in neighbouring FAO Divisions 37.1.1 and 37.1.3. (**) MeHg for cephalopods in FAO Division 37.3.1 are estimated by taking the arithmetic mean of mean MeHg values for cephalopods in neighbouring FAO Divisions 37.2.2 and 37.3.1. The prefixes S_ and L_ denote small (trophic level < 4) and large (trophic level ≥ 4) demersal (DF) and pelagic fish (PF) respectively.

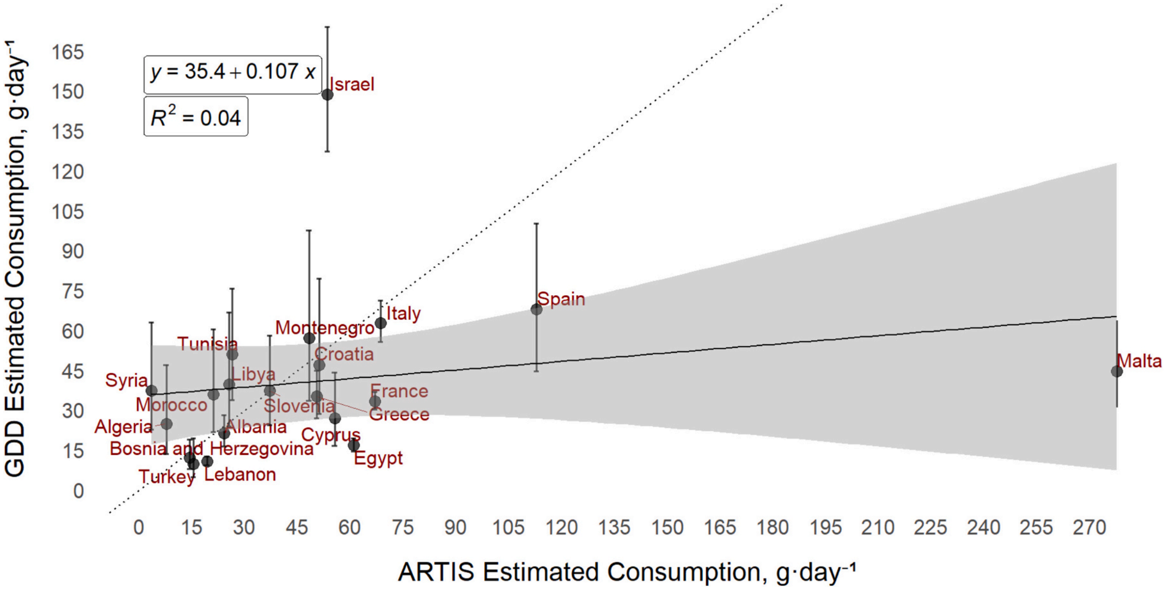

Fig. 3. Mean daily seafood consumption (g · adult^{-1} · day^{-1}) in Mediterranean countries: ARTIS vs GDD. Total seafood consumption corresponds to seafood of all origins for adult populations between 15 and 64 years in 2019. The value for GDD is obtained by computing the population-weighted average consumption for corresponding age groups, with consumption and population size provided by GDD and IHME datasets respectively. The value for ARTIS corresponds to total supply divided by total population size aged between 15 and 64 years as provided by ARTIS and IHME datasets respectively. Error bars represent SD.

distinguish between different types of seafood and role of international trade in order to improve the accuracy of the estimates and provide deeper insights into population exposures.

3.3. *Mediterranean population's MeHg exposure*

The results (Fig. 5) demonstrate that the estimated weekly MeHg intakes (EWI) may exceed the JEFCA's provisional tolerable weekly intakes (PTWI) of 1.6 μg · [kg BW]$^{-1}$ · week^{-1} only in high contamination scenarios based on 75th and 90th percentiles for such countries as Tunisia, Libya, and Algeria that heavily rely on consumption of locally captured seafood. The rest of the Mediterranean countries are within the tolerable limits when taking international trade into consideration. This is a reasonable estimate since the Mediterranean region is not the only region that consumes and provides seafood supply to Mediterranean countries.

It's important to note, however, that despite representing only a small fraction of local consumption for most Mediterranean countries, Mediterranean seafood already contributes to almost half of the recommended PTWI. Exposures could be considerably higher if seafood from other FAO Divisions were included, or if coastal consumers were feeding mostly locally caught seafood. Expanding the methodology in this direction would be a next logical step towards achieving a more comprehensive analysis of population exposures.

3.4. *Economic costs of IQ loss associated with MeHg exposures*

Fig. 6 presents the estimated economic costs associated with IQ loss due to MeHg exposure in newborns across Mediterranean countries in 2019. When summing across all Mediterranean countries, those costs could exceed €10 billion. The analysis includes both GDP per capita (GDPpc)-adjusted and purchasing power parity (PPP)-adjusted values to account for differences in labor productivity and price levels between countries.

The highest economic impacts are observed in larger countries, with Egypt, France, Turkey, Italy, Algeria, Morocco showing the greatest total costs, exceeding €1 billion in both adjustment types, followed by Lebanon and Spain. When adjusted for productivity differences the

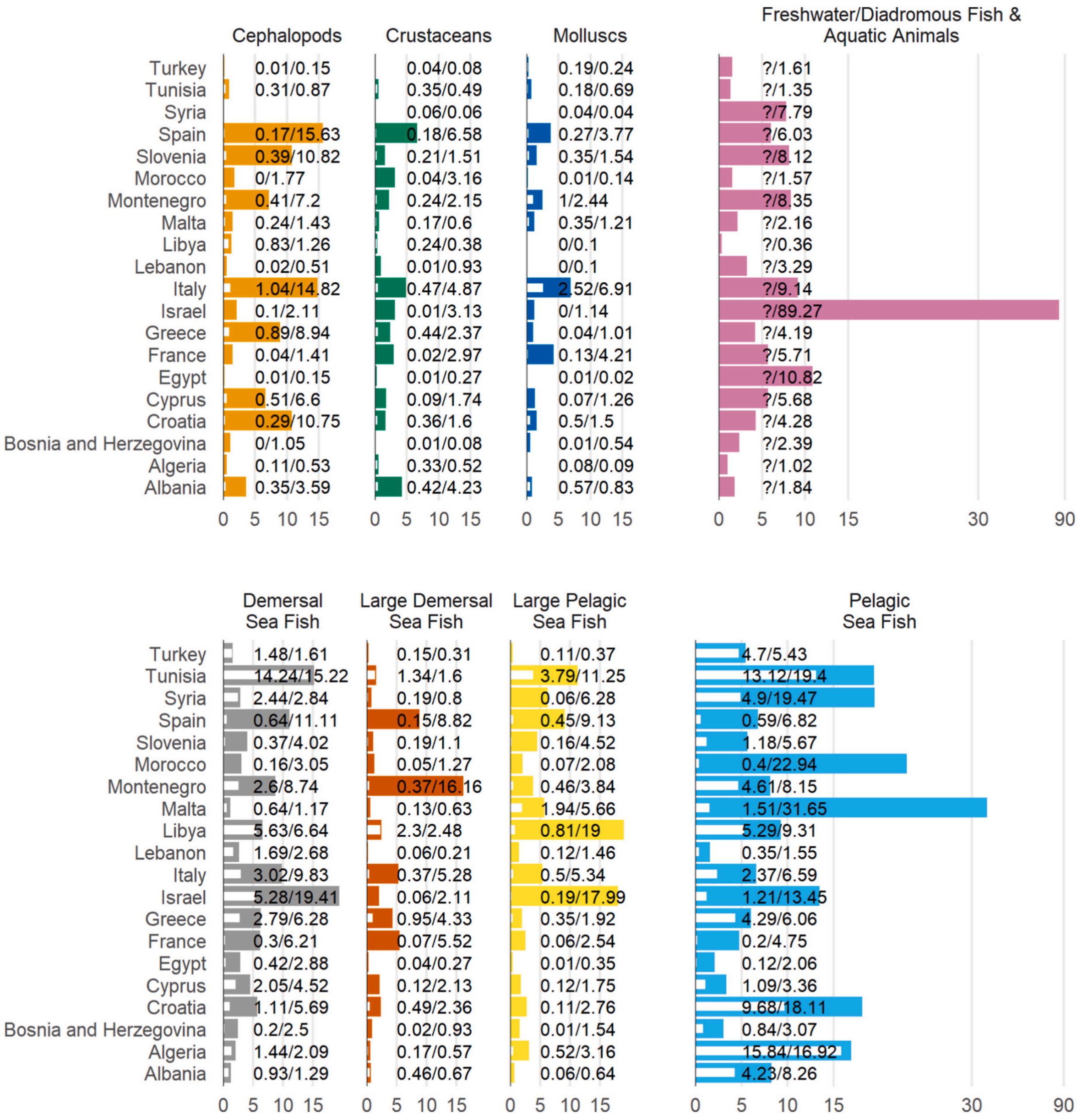

Fig. 4. Mean daily adult seafood consumption in Mediterranean countries [g · adult^{-1} · day^{-1}]: originating in Mediterranean, Black, and Marmara Seas (white bars) vs Total (colored bars). The daily adult seafood consumption covers ages between 15 and 64 and is reported as population-weighted average consumption for corresponding age groups, with consumption and population size provided by GDD and IHME datasets respectively. To account for seafood trade, consumption values of each category were estimated by combining information on total seafood consumption from GDD database, consumption structure and provenance from ARTIS database, as well as FAO Division of production from FAO regional capture statistics for each Mediterranean country.

situation remains relatively stable with such countries as Turkey, France, and Egypt staying at the top and surpassing €2.2 billion in economic costs.

Smaller Mediterranean nations, including Albania, Cyprus, Bosnia and Herzegovina, Malta and others, show significantly lower costs, all falling below €0.3 billion. The differences between GDPpc and PPP adjustments are generally minimal for these countries, suggesting less variation in labour productivity and price differences. The divergence between GDPpc- and PPP-adjusted costs becomes more pronounced in countries like Turkey, Lebanon, Morocco where some countries display higher PPP-adjusted values indicating that price level differences play a more significant role in these economies.

Overall, the total economic burden of IQ loss due to MeHg exposure varies widely across the Mediterranean with more fertile and exposed nations bearing the highest absolute costs. These estimates underscore the economic impact of MeHg exposure and highlight the importance of considering both labor productivity and price differences in assessing the full economic costs across diverse regions.

4. Discussion

4.1. Seafood contamination

In the context of Mediterranean fisheries stocks, it appears that larger species are more often heavily contaminated with MeHg in comparison to their smaller counterparts. For instance, while only 14.4 % of non-carnivorous fish, molluscs and crustaceans' samples displayed unsafe seafood MeHg levels (above the recommended 0.5 μg · g^{-1} WW by the JECFA), top predator fish (ex: tuna, swordfish, sharks, etc.) and cephalopods samples exceeded the safety threshold of 1 μg · g^{-1} WW in 16.3 %

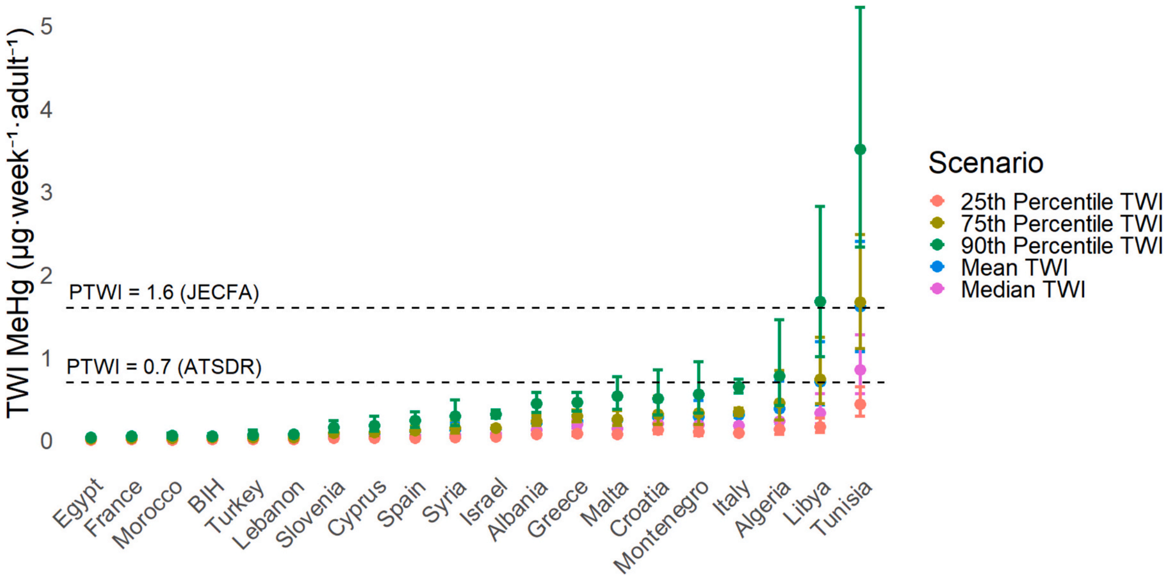

Fig. 5. Estimated Weekly MeHg Intake via seafood of Mediterranean origin (μg · [kg BW]$^{-1}$ · week^{-1}) in adult Mediterranean populations. The horizontal lines show the "Provisional Tolerable Weekly Intake" set by ATSDR and JECFA.

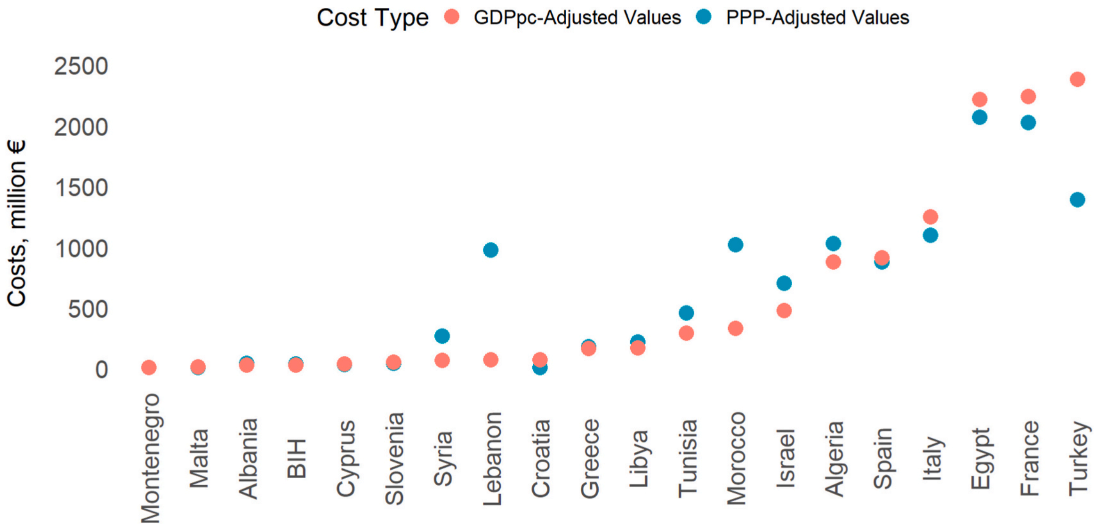

Fig. 6. Economic costs due to lost economic productivity resulting from MeHg-associated cognitive deficits, reported in million EUR.

of the cases. This finding supports previous studies showing that MeHg concentrations in larger species of Mediterranean seafood products would be unsafe for consumption (Damiano et al., 2011; Girolametti et al., 2022; Tseng et al., 2021). This finding once again confirms that smaller fish are to be preferred whenever possible.

We also found large differences in MeHg contamination among seafood categories. Indeed, cephalopods and other molluscs tend to have smaller and generally consistent MeHg levels across regions, suggesting that they are a relatively safe seafood option. Crustaceans and fish above trophic level of 4 exhibit relatively higher MeHg levels. An analysis on non-carnivorous fish stocks from Western Mediterranean islands similarly revealed that 40 % of non-carnivorous fish had mercury concentrations above the EU recommended values (Junqué et al., 2018). On the other hand, fish higher up the trophic level chain present the highest MeHg concentrations. This study agrees with relevant literature that Mediterranean seafood products, particularly top predator fish products such as tunas, swordfish and sharks pose significant health risks to consumers. Overall, there are noticeable regional differences, with higher contamination levels generally observed in the Gulf of Lions and Adriatic regions. These findings underscore the importance of considering both seafood type and geographical variability in exposure risk assessments, with special attention to high-risk species such as large pelagic and large demersal fish in regions where contamination is more pronounced.

The MeHg levels compiled in this study database varied greatly between species and between individuals of the sample species. Considering all species, the MeHg levels ranged from 0.00024 and 23.6 μg · g^{-1} WW. This inter-species variability is the result of two complex processes driving the distribution of MeHg in the trophic webs. Firstly, MeHg levels increase in an organism during its lifetime (bioaccumulation). Secondly, MeHg levels increase from prey to predator throughout food webs (Biton-Porsmoguer et al., 2022). To demonstrate the high intra-species variability, the Mediterranean mussel (*Mytilus galloprovincialis*) showed the highest range of MeHg contamination (from 0.001 to 23.6 μg · g^{-1} WW). This range could potentially be explained by the many measurements taken throughout the Mediterranean with different levels of pollution because the Mediterranean mussel is a frequently studied bioindicator considering its major role as a filter feeder and aquaculture species. Biological factors (such as type of diet, body mass, age, etc.) and ecological factors like the biological habitat can also explain why species display variable MeHg contamination levels (Renieri et al., 2014). Further research could use this study's database to assess mercury levels species by species and establish a list of “safe Mediterranean seafood products” that always meet seafood safety requirements for human consumption. A list of 13 “safe” species including European sardine (*Sardina pilchardus*), European anchovy (*Engraulis encrasicolus*), blue whiting (*Micromesistius poutassou*), picarel (*Spicara smaris*), etc., has already been established for the Western Mediterranean FAO fishing zone (Capodiferro et al., 2022). Future studies could prepare a similar list for the remaining Mediterranean FAO fishing zones and could include other small pelagic and medium sized fish.

Our methodology based on an exhaustive scientific literature review enabled the estimation of MeHg levels at the scale of the Mediterranean without conducting costly field missions. However, this approach has several limitations. Firstly, the median levels of MeHg estimated for fish can present sample bias. Several factors can contribute to the high levels of estimated MeHg in fish and seafood products. The Mediterranean waters exhibit high propensity for methylation, where MeHg can make up as much as 86 % of the total mercury content. Consequently, fish species in the Mediterranean accumulate higher levels of Hg compared to those in the Atlantic, a phenomenon known as the ‘Mediterranean mercury anomaly’ (Cossa and Coquery, 2005). Increasing temporal trend in Hg concentration is observed in the Mediterranean and the difference in Hg concentration between the Mediterranean and the Atlantic species is particularly pronounced in larger predatory species, with for instance average values in lean fish collected off of Spain of 1.5 $\mu g \cdot g^{-1}$ WW and 0.43 $\mu g \cdot g^{-1}$ WW, respectively (Junqué et al., 2018). This study identified several species that exceeded the maximum mercury limits stipulated by Regulation (CE) 1881/2006, predominantly including tunas, sharks, and swordfish. It's worth noting that smaller species, primarily benthic ones, were also found to exceed the threshold of 0.5 $mg \cdot kg^{-1}$ but not as frequently as their larger counterparts.

Another factor that can lead to elevated mercury levels may stem from particularly high levels of mercury local pollution. Alternatively, it could arise from a statistical bias that may occur when certain species, such as bottom dwellers, older specimens or top predators, which tend to accumulate larger amounts of MeHg are predominantly sampled (Renieri et al., 2014). Consequently, if those species represent a significant number of samples in a specific fishing division, it can artificially increase the calculated median MeHg levels in fish seafood products. We attempt to resolve this potential bias by distinguishing small and large fish based on its trophic levels. Finally, the median MeHg contamination levels estimated in this study might not be representative of every Mediterranean region due to insufficient samples. For example, out of the 17,934 measurements, only 5 data points were available for crustaceans fished in the Gulf of Lions, while cephalopods had to be extrapolated the Gulf of Lion and Aegean Sea because of the lack of observations in these FAO Divisions. Moreover, there was less data in the Aegean Sea which only represented 3.88 % of the total samples. This suggests a need for more extensive and continuous monitoring of mercury levels in some Mediterranean regions more than others.

4.2. Seafood consumption

In the present study, we use GDD consumption estimates adjusted to 2019. According to it, Israel, Spain and Italy exhibit the highest seafood consumption rates per adult. Italy, Slovenia, Cyprus, and Spain mostly consume cephalopods and other molluscs (around 20 $g \cdot adult^{-1} \cdot day^{-1}$which is equivalent to around 30 % of total seafood consumption). Albania displays the highest consumption share of crustaceans (19 %), followed by Spain, and France (around 4–6 $g \cdot adult^{-1} \cdot day^{-1}$). Syria, Egypt, Tunisia, Libya, Algeria, and Malta have the highest share of fish consumption above 90 %. Overall, the results support other studies stating that Spain, France and Italy have the highest per capita seafood consumption (Dincer, 2017; WWF, 2017).

The study also reveals the differences in consumption patterns across countries which can be attributed to the type of seafood industry. Spain, France and Italy have intensive fishing methods and associated preservation, processing, and transportation industries. This facilitates a more homogeneous consumption of seafood throughout the population (Višnjevec et al., 2014). On the contrary, Greece has less industrialized, more labour-intensive and artisanal small-scale fisheries whose products are consumed locally (FAO, 2020). This is supported by findings that show countries without intensive seafood industries have considerable consumption level differences between coastal and inland populations (Višnjevec et al., 2014). Furthermore, other reasons such as cultural and gastronomic preferences, country, demography, standards of life, etc. that are unique to each country could further explain different seafood consumption patterns (Višnjevec et al., 2014).

Considering that seafood supply data is not the ideal source of data to conduct exposure assessments, our methodology combines both consumption structure and its provenance with consumption survey data while also applying edible conversion factors to ensure the comparability of different datasets. Nevertheless, the methodology still presents limitations. It does not account for spoilage or household waste which can be significant. It does not account for differences in food consumption patterns among the population based on age, gender, region, etc. Additionally, the distribution of seafood consumption among consumers is estimated and does not differentiate between high and low quantity seafood consumers. Lastly, while we are able to distinguish the seafood provenance, we estimate only a small fraction of total consumption given that the share of imported products is quite high in many Mediterranean countries as demonstrated by ARTIS data.

Therefore, future research should validate the methodology proposed in this study and develop more comprehensive estimates of global exposure levels by considering all dietary sources of MeHg. This approach will help safeguard public health by enabling more precise and efficient assessments of exposure risks.

4.3. Exposure

As we've previously demonstrated, MeHg exposures are especially high in Tunisia, Libya, and Algeria. In these countries, population diets heavily rely on local small-scale fisheries products (FAO, 2020). The last United Nations Global Mercury Assessment (GMA) (UN Environment, 2019) compiled several population studies (e.g. National human biomonitoring programs, Longitudinal birth cohort studies and Cross-sectional studies on vulnerable populations) that were conducted in some of the Mediterranean countries. In agreement with our findings, this report states that coastal populations who substantially depend on local seafood are more vulnerable to high levels of MeHg exposure.

Furthermore, given high levels of MeHg in Mediterranean seafood, its excessive consumption may pose serious health risks not only in the Mediterranean, but also across the world. Our analysis has demonstrated that most Mediterranean countries transfer a large portion of their contamination via international trade and consequently consume less contaminated seafood of foreign origin. This explains the lower impact of Mediterranean seafood in the Mediterranean region. However, the transfer of risks does not necessarily imply their elimination. Firstly, as mentioned earlier, our analysis does not distinguish between low and high quantity consumers which would underestimate exposure in countries with lots of high quantity consumers and vice versa. Secondly, while in theory it could happen that countries exchange in a way which ensures that everyone is exposed to the same levels of contamination, it is not necessarily the case in practice. Thus, further research needs to verify it by compiling MeHg estimates for the rest of FAO Divisions and incorporating them into comprehensive analysis.

Finally, using dietary data may have led to biased exposure estimates given that there may be substantial heterogeneity in absorption levels in various populations. To check the relevance of our results, future studies should validate the results using epidemiological data including such biomarkers as blood/hair MeHg levels (for instance, the data from DEMOCOPHES project (LIFE09 ENV/BE/000410) could be used for such purposes in European countries) (Bellanger et al., 2013).

4.4. Costs-of-illness analysis

Cost-of-Illness analysis in this study further demonstrates the benefits of environmental disease prevention. While based on the estimates of expected lifetime earnings at birth in the United States, we attempt to correct for country differences by using PPP-adjustment and GDP per capita adjustment approaches that have often been used in the literature for those purposes.

However, our first estimate is likely an underestimation, as it excludes seafood of non-Mediterranean origins. Yet, we had to exclude it from our analysis to achieve the necessary level of detail since the level of contamination in different seas and oceans is not necessarily the same. For instance, numerous studies demonstrate that the Mediterranean Sea is more contaminated, thus, we cannot apply MeHg levels found in the Mediterranean Sea to the whole seafood supply. At the same time, the only contamination that we can feasibly compute is related to the seafood produced in the Mediterranean because the contamination database at our disposal was specifically compiled for the Mediterranean Sea. The analysis is further complicated by international trade since we can no longer say that everything that was locally produced is also consumed by local populations. For this reason, taking provenance aspects into account allows us to provide more accurate results but limits the scope of the study because to provide a full picture we also need to know contamination of seafood sourced from other seas and oceans. Furthermore, as noted in (Bellanger et al., 2013), we do not consider direct medical expenses for treating neurodevelopmental disorders in children or indirect costs related to special education and extended schooling. Additionally, potential long-term benefits, such as those from reduced cardiovascular or neurodegenerative effects of MeHg exposure—especially relevant for high fish consumers—are difficult to quantify and were not included. Any compensation of the IQ benefit due to special education and other remedies were not considered either. Finally, these calculations do not account for the less tangible benefits of protecting brain development from neurotoxicity, as along with preventing other adverse effects and unnecessary suffering. Considering those elements would allow us to obtain more accurate results but the lack of data and difficulty in estimating intangible benefits requires us to compromise some accuracy in terms of economic costs. Nonetheless, the result provides the first provisional point of reference for policymakers and emphasizes the importance of international cooperation for optimizing the mitigation of exposures to toxic agents on the global scale.

Seafood is one of the most globally traded food commodities, and international trade plays a pivotal role in the redistribution of both nutrients and contaminants such as methylmercury (MeHg). In the context of the Mediterranean Sea, fishing products contribute significantly to international seafood markets, with large portions of the catch being exported to non-regional destinations. At the same time, Mediterranean countries also rely on seafood imports, which can alter the MeHg exposure of local populations.

Using the Aquatic Resource Trade in Species (ARTIS) database, we analyzed seafood trade flows to and from the Mediterranean region. This database allowed us to capture detailed information on the origin and destination of seafood products, including trade volumes and species composition. By integrating ARTIS data with MeHg concentration estimates, we assessed how trade influences the diffusion of MeHg between countries.

Our results indicate that approximately 16.46 % of the seafood harvested in the Mediterranean is exported to markets outside the region, redistributing MeHg contamination globally. Conversely, imports from lower-contamination regions (e.g., North Atlantic or Southeast Asia) will contribute to a reduction in dietary MeHg exposure in certain Mediterranean countries.

The redistribution of MeHg through trade underscores the need for international monitoring systems, robust food safety standards and stronger policies for traceability, to ensure global public health protection. For Mediterranean countries, where seafood represents a cultural and dietary staple, there is an urgent need for policies that balance the promotion of sustainable fishing practices with public health protection. Additionally, regional collaborations could harmonize standards for MeHg monitoring, data sharing, and exposure reduction strategies to protect populations most at risk. By highlighting the interplay between international trade and MeHg redistribution, this study provides a framework for policymakers to address these challenges in a globalized food system, ultimately safeguarding public health while supporting sustainable seafood production and trade practices.

5. Conclusion

In this study, we have developed a new methodology for estimating population exposures combining the results of consumption surveys from Global Dietary Database (GDD) and recently published dataset on Aquatic Resource Trade in Species (ARTIS) which not only harmonizes the available seafood supply data but also accounts for its provenance (origins) and composition allowing to perform a more granular analysis. The comprehensive MeHg dataset collected for this study, spanning four decades, has further provided us with a deeper understanding of mercury distributions in Mediterranean seafood and its impact on adult exposures in Mediterranean countries taking into account the impact of international trade.

Our study offers invaluable insights for policymakers by providing novel estimations of the economic and societal costs associated with mercury pollution in the Mediterranean region. Such estimates justify investments in pollution prevention. Furthermore, as it continues to be refined, the approach developed in this study has the potential to greatly improve the assessment of chemical exposure from seafood by offering a common framework that is transferable to other regions. Finally, the study provides leeway for further research, as the methodology applied may be used for investigating the impact of other contaminants.

CRediT authorship contribution statement

James Kennedy: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation. **Emma Calikanzaros:** Writing – review & editing, Writing – original draft, Methodology, Conceptualization. **Philip J. Landrigan:** Writing – review & editing, Methodology, Conceptualization. **Pierre-Marie Badot:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Mine Cinar:** Writing – original draft, Conceptualization. **Alain Safa:** Writing – review & editing, Conceptualization. **Rahel M. Schomaker:** Writing – review & editing, Methodology, Conceptualization. **Josep Lloret:** Writing – review & editing, Writing – original draft, Methodology, Conceptualization. **Hervé Raps:** Writing – review & editing, Methodology, Conceptualization. **Marie-Fanny Racault:** Writing – review & editing, Methodology, Conceptualization. **Nathalie Hilmi:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Funding acquisition, Formal analysis, Conceptualization. **Marie Yasmine Dechraoui Bottein:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization, Validation, Project administration.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used Chat GPTin order to assist with English language correction. After using this tool/

service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2024.177953.

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