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Nutrition

Selenium health benefit values provide a reliable index of seafood benefits vs. risks

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ABSTRACT

Background: Methylmercury (CH_3Hg) toxicity causes irreversible inhibition of selenium (Se)-dependent enzymes, including those that are required to prevent and reverse oxidative damage in the brain. Fish consumption provides numerous essential nutrients required for optimal health, but is also associated with CH_3Hg exposure risks, especially during fetal development. Therefore, it is necessary to assess the amounts of both elements in seafood to evaluate relative risks or benefits. Consumption of ocean fish containing Se in molar excess of CH_3Hg will prevent interruption of selenoenzyme activities, thereby alleviating Hg-exposure risks. Because dietary Se is a pivotal determinant of CH_3Hg's effects, the Selenium Health Benefit Value (HBV) criterion was developed to predict risks or benefits as a result of seafood consumption. A negative HBV indicates Hg is present in molar excess of Se and may impair Se availability while a positive HBV indicates consumption will improve the Se status of the consumer, thus negating risks of Hg toxicity.
Objective: This study examined the Hg and Se contents of varieties of seafood to establish those with positive HBV's offering benefits and those having negative HBVs indicating potential consumption risks.
Methods: The Hg and Se molar concentrations in samples of meat from pilot whale, mako shark, thresher shark, swordfish, bigeye tuna, and skipjack tuna were used to determine their HBV's in relation to body weight.
Results: The HBVs of pilot whale, mako shark, and swordfish were typically negative and inversely related to body weight, indicating their consumption may impair Se availability. However, the HBV's of thresher shark, bigeye tuna, and skipjack tuna were uniformly positive regardless of body weights, indicating their consumption counteracts Hg-dependent risks of selenoenzyme impairment.
Conclusions: The HBV criterion provides a reliable basis for differentiating seafoods whose intake should be limited during pregnancy from those that should be consumed to obtain health benefits.

1. Introduction

Selenium (Se) is an essential trace element that is required for synthesis of selenocysteine (Sec), the 21st genetically encoded amino acid required for the activities of selenoenzymes with critical roles in fetal brain development, growth, thyroid hormone metabolism, calcium regulation and prevention/reversal of oxidative damage. [1–8] The importance of Se for brain functions is emphasized by the fact that highly conserved mechanisms have evolved to maintain optimal brain Se concentrations even when dietary Se intakes are deficient. Because the brain is preferentially supplied [9–11], its Se concentrations are maintained near normal (˜1 μM) even when prolonged exposures to Se-deficient diets diminish Se concentrations in somatic tissues such as blood or liver to ˜2% of their normal levels [2].

Numerous studies have shown dietary Se counteracts methylmercury (CH_3Hg) toxicity [12–18] and the protective effect of Se from ocean fish consumption against CH_3Hg, toxicity has been repeatedly shown in laboratory animals. [19–24] Serious impairments of brain Se and selenoenzyme activities are only known to occur as a result of genetic knockouts of Se-transport/uptake proteins [10,25,26], or following high CH_3Hg exposures. [24,27,28], The ability of Se to decrease or abolish the toxic effects of high Hg exposures has been well established [29–32] and it is now understood that the mechanism of CH_3Hg toxicity primarily occurs through disruption of brain Se metabolism. [5,33–38] Prior to recognition of CH_3Hg's role in inhibiting selenoenzyme metabolism, the mechanism of CH_3Hg toxicity was thought

Abbreviations: HBV, health benefit value; Hg, mercury; CH_3Hg, methylmercury; HgSe, mercury selenide; ppm, parts per million; PCB, polychlorobiphenyls; Se, selenium

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to involve its high affinity for thiols (10 [39]) and arise due to disruption of sulfur metabolism. Sulfur is far more abundant in tissues than Se (˜300,000:1), but Hg's association constant for Se (10 [45]) is ˜1 million times higher than its affinity for sulfur [39]. Due to their high tissue concentrations, thiomolecules bind CH_3Hg initially, but because they are substrates for selenoenzymes, they directly deliver CH_3Hg into enzyme's active site in the proper orientation to bring the Hg moiety into close proximity with the Se of the catalytic Sec residue. The CH_3Hg transfers from the thiol to the Sec, forming a CH_3Hg-Sec which is degraded into Hg selenide (HgSe), a virtually insoluble (solubility constant 10^{-58} to 10^{-65}) and therefore biologically unavailable form of Se, [39] which can contribute to a functional Se deficiency if Hg sequestration rates outpace Se transport into the tissue.

An important aspect of dietary CH_3Hg is its ability to cross placental and blood-brain barriers to irreversibly inhibit selenoenzyme activities in the fetal brain. [27,28,42] Therefore, high CH_3Hg exposures during pregnancy are a concern if dietary Se intakes are not adequate to offset losses due to Hg sequestration. Maternal CH_3Hg exposures from eating seafoods with high Hg:Se molar ratios such as certain types of shark [43] or pilot whale meats and blubber [44–47]have been reported as having subtle adverse effects on child neurodevelopment. Conversely, maternal consumption of ocean fish that contain more Se than Hg has not been associated with health risks, but instead offers health benefits [48–57]. With few exceptions, ocean fish contain more Se than Hg [58] and are abundant sources of important nutrients required for fetal development [48,49,59]. Therefore, since most ocean fish are rich sources of dietary Se, there is protection against the CH_3Hg they contain.

The Health-Benefit-Value (HBV) indicates the relative molar contents of Se and Hg that are present in a food. [36,40, 41,58,60] Most seafoods have positive HBV's indicating Se is present in molar excess of their CH_3Hg contents, while negative values indicate they contain CH_3Hg in excess of Se. [58,61] For example, pilot whale muscle meat samples have Hg contents (3.31 μg/g; 16.4 μmol/kg) that are far higher than their Se (0.25 μg/g; 3.1 μmol/kg) concentrations (Hg:Se molar ratios ˜5:1). [62] Since these results are from the 1977 pilot whale data set which was used to estimate maternal Hg exposures in the Faroe Islands [44], (the population study which was used to establish maternal seafood consumption advice) it is important to compare the Hg and Se contents of pilot whales to representative varieties of ocean fish. To establish reference ranges of positive and negative HBV seafoods in relation to their body weights, this study compared the molar concentrations of Hg and Se in pilot whale, mako shark, thresher shark, swordfish, bigeye tuna, and skipjack tuna muscle meats.

2. Methods

Because shark and pilot whale meats were the dominant source of Hg in studies which reported finding harmful effects, this study compared their HBVs to those of a selection of commonly consumed varieties of ocean fish. The ocean fish data evaluated in this study are from samples of edible fish portions collected in 2006 from commercial landings of pelagic fish as reported in Kaneko and Ralston. [58] Briefly, fish harvested from the central Pacific were weighed and 100 g samples of edible muscle from the anterior portion of the dorsal muscle mass were stored frozen in trace metal free plastic bags. Chain of custody was maintained from the time the samples were collected until they were analyzed for Hg and Se. Sample aliquots of ˜0.4 g (wet weight) weighed to 0.0001 g from each sample were transferred into single use trace element free 50 mL digestion tubes (Environmental Express, Mt Pleasant, SC 29464) with every tenth fish sample being prepared in duplicate and with elemental spike recovery samples being performed accompanying each batch. Each digestion batch was processed with blank and certified standard reference materials (dogfish muscle certified reference material DORM-2, National Research Council of Canada, Ottawa, Ontario Canada). Samples were treated with 5 mL of 16 N nitric acid (Fisher Trace Metal Grade, Fisher Scientific, www.fishersci.com) and heated at 85 °C in deep cell hot blocks (Environmental Express, Mt. Pleasant, SC) for 24 h in capped tubes. Samples were cooled and 1.5 mL of 30% H_2O_2 (Fisher Certified A.C.S., Fisher Scientific, www.fishersci.com) were added. Samples were heated at 90 °C for 90 min to reduce Se-VI to Se-IV, then cooled and diluted to 50 mL with double distilled water. Samples were analyzed for Hg content by cold vapor atomic absorption spectrophotometry using a CETAC M-6000A (CETAC Technologies Inc, Omaha, NE), and Se was analyzed by hydride generation atomic fluorescence spectroscopy using a PS Analytical Dual Millennium Excalibur, (PS Analytical, Deerfield Beach, FL). The Hg and Se molar concentrations of these samples were used to calculate their HBV's and Se deficits or excess were evaluated in relation to body weights.

The large sizes of pilot whales (*Globicephala melas)* precluded weighing to establish body mass. As reported in the original literature, [62] their mass was recorded on the basis of "skinns" (a traditional apportionment term) rather than body weights. A 75 kg skinn corresponds to ˜50 kg of meat and ˜25 kg of blubber along with varying amounts of liver and kidney corresponding to an estimated intake ratio of 65:32:3 for muscle meat, blubber, and liver respectively; the amount of kidney consumed was not reported [63]. Male pilot whales have a maximum body weight of ˜2300 kg and females are up to ˜1300 kg.[64] Therefore, to estimate pilot whale body weights, the number of skinns per whale was multiplied by 1.9; a factor that was determined to provide approximations that conform with their normal weight range. This resulted in a mean estimated adult body weight of ˜1187 kg, with the largest whale having a value of 2280 kg, values which correspond to reference weights reported for this species.

The Hg and Se mass concentrations (mg/kg) were converted to molar concentrations (μmole/kg), and results were evaluated. The concentrations of Hg and Se in individual fish and whale meat samples were used to calculate corresponding HBVs using the equation described in Ralston et al., 2016: [35]

((1)) $HBV = (Se - Hg)/Se \cdot (Se + Hg)$

The molar excess of Se ("free" Se) present in the samples was determined by subtracting the molar Hg concentration from the molar Se concentration for individual samples. Means and standard deviations of elemental molar concentrations, HBV's, and Se excess or deficits were calculated, graphed, and evaluated.

3. Results

The reference material used for Hg and Se in fish tissue was (DORM-2) dogfish (freeze dried powdered Squalus acanthias) muscle obtained from the National Research Council of Canada, with reference values of 1.40 ± 0.09 μg Se/g and 4.47 ± 0.32 μg Hg/g (dry weight basis). We observed that Hg recovery was inversely related to the amount of sample digested ($p = 0.05$), $F = 6.91$, Adjusted $R^2 = 0.54$. While 100 mg (or less) of DORM-2 provided recoveries of ˜99.9%, Hg recoveries declined as the amount of sample increased. For example; 150 mg provided a recovery of 95.4 ± 0.2% and 200 mg provided a recovery of 90.8 ± 0.7%. This effect was not observed for Se recoveries from DORM-2. Additionally, inclusion of HCl in addition to HNO_3 in a quantity approximating aqua regia proportions was essential for complete recoveries. The observed Se (1.36 ± 0.04 ug/g; 97 ± 3% of certified value), and Hg contents (4.32 ± 0.38 ug/g; 97 ± 9% of certified value) indicated the elemental recoveries were reliable and replicate sample analyses indicated adequate precision. While digestion blank values for Hg were sufficiently low to be considered negligible, digestion blank Se contents (0.49 ± 0.17 ng/ml) were subtracted prior to calculating Se contents of samples.

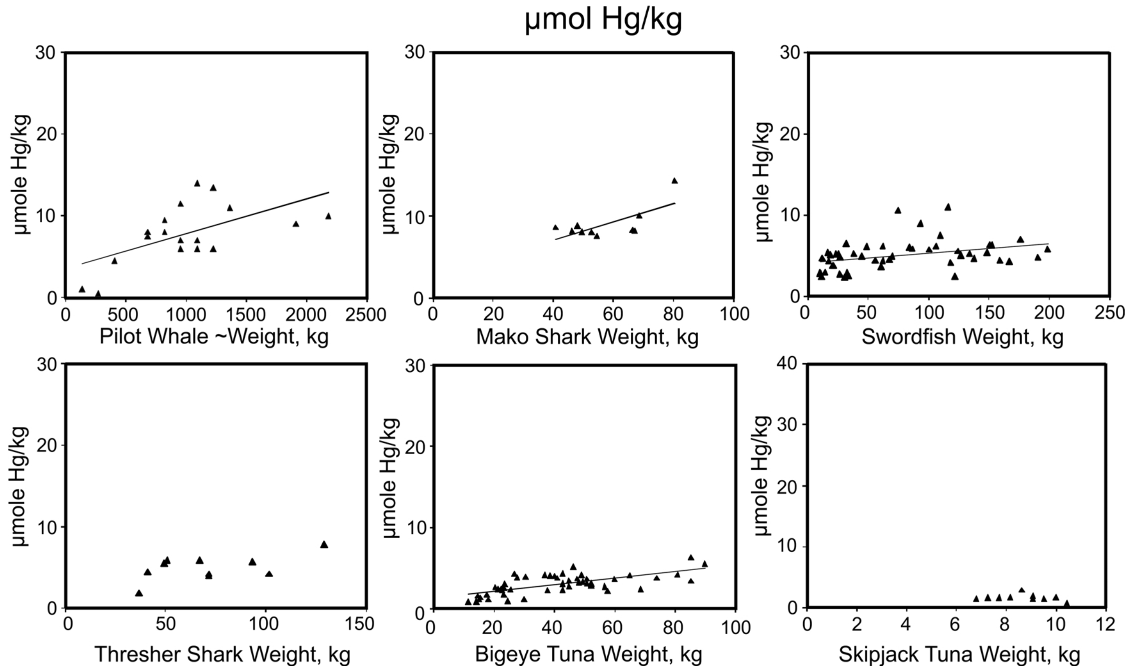

Fig. 1. Total Hg concentrations (μmol/kg) for the seafoods assessed in this study.

3.1. Pilot whales

The Hg contents of pilot whale meats uniformly exceeded Se contents on a molar basis in adult animals (Fig. 1, Fig. 3, Table 2). The amount of Hg increased in direct relation to body size (See Table 1 and Fig. 1). Aside from the higher Se contents noted in fetal pilot whales (not shown) and very young calves, total Se contents were not associated with body size (Fig. 2). This is consistent with previous findings that homeostatic controls regulate tissue Se, thus body size does not typically affect the amount of Se present, although HgSe accumulation can increase in certain tissues. [65] Aside from samples of one adult and two young calves, the HBV's of pilot whale meat were negative and significantly diminished ($p = 0.01$; $F = 9.1$) as body size increased (Fig. 2, Table 2). Since Hg bioaccumulation was directly associated with body size of pilot whales (Fig. 3), the calculated Se-deficit associated with these samples was directly related to their Hg contents ($p < 0.01$; $F = 12.7$). Males of this species live up to ˜40 years and attain maximal weights of ˜2300 kg while females live up to 60 years and attain maximal weights of ˜1300 kg. [64] Although the sex of the assessed samples was not available, this sexual dimorphism may be evident in the Hg accumulation and HBV distribution patterns noted in pilot whales (Figs. 1 and 2).

3.2. Mako sharks

The Hg contents of mako shark were directly related to their body size (Table 1, Fig. 1). The HBV of all samples included in this assessment were uniformly negative (Fig. 2, Table 2). Although the HBV of these samples tended to decline as body size increased, the relationship was not significant ($p = 0.11$), possibly because only 10 samples were assessed and the range of sample body weights examined was relatively narrow (40–80 kg). However, like pilot whales, mako shark meat contained more Hg than Se, and Se-deficits (Fig. 3) were directly associated with increasing Hg contents ($p < 0.001$; $F = 139.9$).

3.3. Swordfish

The Hg contents of swordfish were directly related to body size (Fig. 1). Although the HBV of the swordfish was positive in many specimens, many samples had negative values (Fig. 2) and there was a tendency for HBV's to decline in relation to increasing size ($p = 0.07$). As a result, the average HBV for swordfish was ˜zero, but highly variable (Fig. 2, Table 2). The Se surplus or deficit was dependent on Hg content ($p < 0.001$; $F = 38.5$), with samples containing Hg in excess of 5 μmol/kg (˜1 mg/kg) having the lowest HBV's (Fig. 3).

3.4. Thresher sharks

The Hg contents in thresher shark tended to increase in relation to increasing body size (Fig. 1) but Se contents were consistently higher in all samples assessed (Fig. 2, Table 2). As a result, the HBV of thresher shark samples were uniformly positive although they declined with increasing body size due to increasing Hg (Fig. 2). Therefore, unlike mako shark, thresher shark meats provide a Se-surplus.

Table 1
Seafood Mercury Contents and Relationships to Body Weight.

Seafood	n	Body Wt.	mg Hg/kg	μmol Hg/kg	Slope (Hg x Wt.)	Adj. R^2	F	p value
Pilot whale	18	992.4 ± 507.6	1.56 ± 0.73	7.75 ± 3.62	0.004(x) + 3.51	0.32	8.93	< 0.01
Mako shark	10	57.4 ± 12.5	1.81 ± 0.40	9.01 ± 1.99	0.111(x) + 2.66	0.41	7.41	0.03
Swordfish	49	80.8 ± 55.8	1.00 ± 0.37	4.99 ± 1.85	0.017(x) + 3.91	0.09	6.16	0.01
Thresher shark	10	71.3 ± 69.4	0.97 ± 0.32	4.86 ± 1.60	0.032(x) + 2.57	0.26	4.24	0.07
Bigeye tuna	50	41.2 ± 20.4	0.60 ± 0.25	3.00 ± 1.23	0.040(x) + 1.34	0.44	39.02	< 0.001
Skipjack tuna	10	8.6 ± 1.2	0.34 ± 0.10	1.67 ± 0.52	NS		NS	NS

Table 2
Seafood Selenium Contents, Selenium Deficit or Surplus, and Health Benefit Values.

Seafood	n	mg Se/kg	μmol Se/kg	(μmol Se-Hg/kg)	HBV
Pilot whale	18	0.41 ± 0.31	5.23 ± 3.88	−2.52 ± 6.40	−14.79 ± 19.98
Mako shark	10	0.32 ± 0.04	4.07 ± 0.48	−4.93 ± 1.79	−16.44 ± 8.57
Swordfish	49	0.43 ± 0.12	5.40 ± 1.48	0.41 ± 1.80	0.28 ± 3.73
Thresher shark	10	0.52 ± 0.12	6.55 ± 1.51	1.68 ± 1.43	2.67 ± 2.04
Bigeye tuna	50	0.99 ± 0.28	12.38 ± 3.47	9.40 ± 3.73	11.47 ± 3.79
Skipjack tuna	10	1.56 ± 0.92	19.83 ± 11.71	18.15 ± 11.74	19.61 ± 11.83

3.5. Bigeye tuna

The Hg contents of bigeye tuna samples were lower than those observed in pilot whale, shark or swordfish (Fig. 1, Table 1). Although their Hg concentrations were directly related to body size (Fig. 1, Table 1), Se contents were higher than Hg in all samples assessed (Fig. 3, Table 2). As a result, their HBV values were uniformly positive (Fig. 2, Table 2). There was a gradual decline in surplus Se ($p = 0.01$;

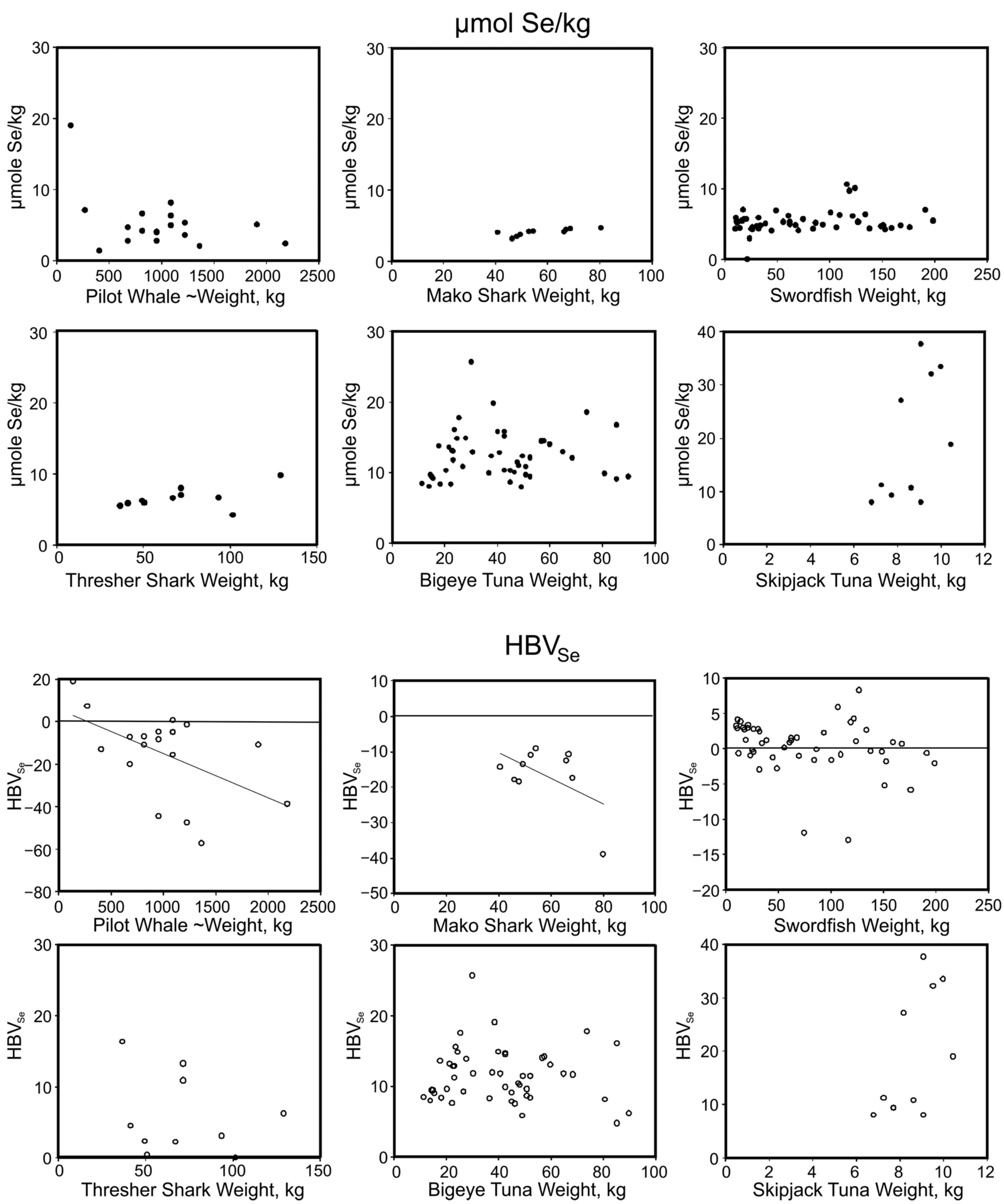

Fig. 2. Total Se concentrations (μmol/kg), and calculated HBVs for the seafoods studied.

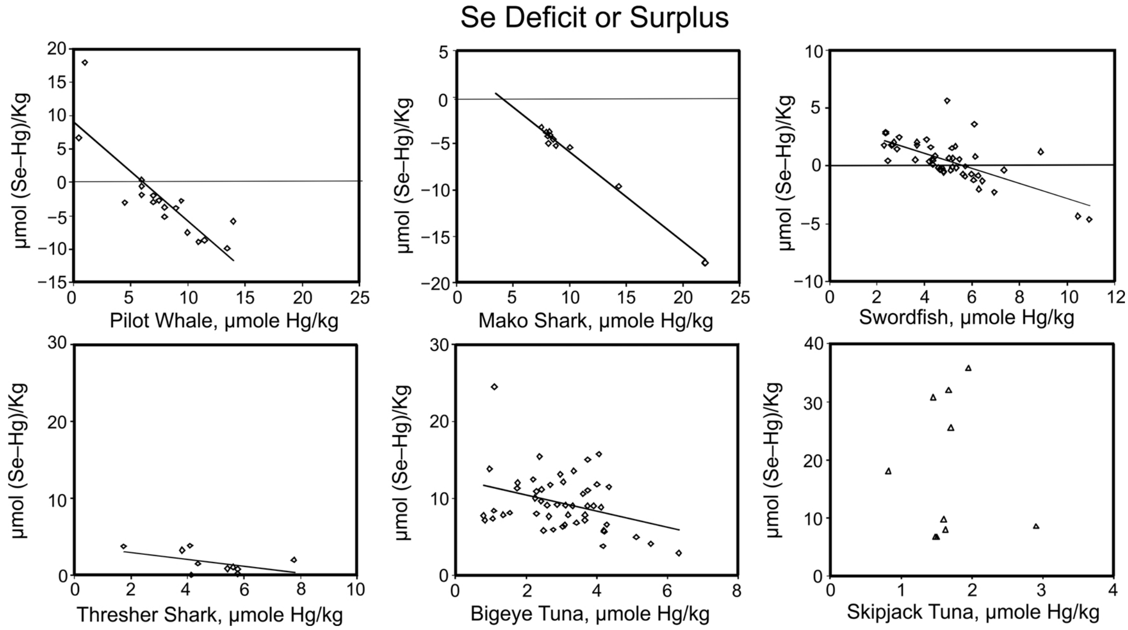

Fig. 3. The relative Se deficit or excess (μmol/kg) shown in relation to seafood Hg contents.

F = 6.8) associated with increasing Hg concentrations, but the values were consistently positive (Fig. 3).

3.6. *Skipjack tuna*

The Hg contents of skipjack tuna were low in comparison to other species assessed in this study and not related to body size (Fig. 1, Table 1). The levels of Se in their tissues were variable and unrelated to body size (Fig. 2). The red meat of skipjack tuna had considerably higher Se contents than the lighter muscle mass (data not shown). The source of this variability is unknown and was not observed in any other varieties of ocean fish studied. The HBV of skipjack tuna were uniformly positive and independent of size (Fig. 2, Table 2). The Se-surplus was not significantly related to Hg or Se concentrations.

4. Discussion

Ocean fish consumption during pregnancy is consistently associated with neurodevelopmental benefits in children compared to those of mothers that avoid fish consumption. [48–57,68], Ocean fish are rich sources of dietary Se [65,66], and although Se contents vary considerably between species, it is generally independent of fish size. However, CH_3Hg concentrations in ocean fish are directly related to their trophic level, age, size, and can vary by orders of magnitude, negatively affecting their HBV (Fig. 2). As shown in Fig. 1, Hg bioaccumulation during early growth is minimal, so HBVs are the highest in the youngest fish (Fig. 2). As their Hg burdens increase, HBV's gradually decline so those with the lowest values tend to be the oldest and largest of their species (Fig. 2). Although the HBV remains positive in even the largest of most fish species, [58] our results indicate this is not the case for pilot whale, mako shark, or swordfish (see Table 1, Fig. 3).

Seafood consumption advisories currently fail to consider Se, and instead of being based on studies that examined the effects of ocean fish consumption, are based on studies of the effects of Hg exposures which primarily originated from consuming pilot whales, not fish. In the Faroe Islands Study, participant consumption of pilot whale meat, blubber, and liver (in proportions ˜65:32:3 [63] were the source of ˜85% of their overall Hg exposures [44,61], The livers (and kidneys) had extremely high Hg and cadmium contents and whale blubber also contained high concentrations of PCB's and all other persistent bioaccumulative toxicants [62,63]. Based on the unusually negative HBV of the pilot whale meat, adverse effects would be expected in children born to mothers who ate pilot whale meat during pregnancy. However, the Hg-dependent Se losses were offset by Se from the ocean fish also consumed, thus alleviating adverse consequences and significant improvements in health outcomes were observed in children whose mothers consumed increasing amounts of ocean fish [67]. These benefits are likely due to Se-restoration along with other positive effects of ocean fish nutrients required for optimal fetal neurodevelopment [48,49,54,55,57,68].

In addition, studies of ocean fish consuming populations have found the children of mothers who ate the most fish during pregnancy had significantly improved neurodevelopmental scores in comparison to those whose mothers ate no fish. [48,49,54,55,57,68] Children in the US whose mothers avoided fish consumption during pregnancy lost IQ benefits [53] that were 60–100 times greater [60] than the worst-case effects reported with Hg exposures from pilot whale consumption in the Faroes. Maternal seafood intake during pregnancy of less than the amount recommended by the 2004 U.S. fish consumption advisory [69]] (340 g per week) was associated with increased risk of their children being in the lowest quartile for verbal intelligence quotient (IQ) compared with mothers who consumed more than 340 g per week. Low maternal seafood intake was also reported to be associated with increased risk of suboptimum outcomes for prosocial behaviour, fine motor, communication, and social development scores. The authors also stated that for each outcome measure, the lower the intake of seafood during pregnancy, the higher the risk of suboptimum developmental outcome. [48] Diminished fish consumption also increased children's risks for pathological scores in fine motor, communication, and social skills. Conversely, increasing maternal fish consumption beyond the reference dose during pregnancy was associated with improved child performance. [48]

To ensure the safety of the most sensitive population subgroups, recommendations based on the HBV criterion are exceedingly cautious in that it considers only the seafood itself, without regard to other Se sources in the diet. Recognizing that dietary intakes account for ˜19.8% of the total variation in maternal blood Hg concentrations [70] while diet is the exclusive source of Se, the margin of safety afforded by the HBV is purposefully cautious. It does not reflect the amounts of Hg bound to other elements or consider the other sources of Se in the diet.

Since seafood consumers generally eat a variety of fish which have positive HBV's and enrich their Se intakes, occasional consumption of a negative HBV seafood is unlikely to diminish Se-status. This may explain why the Faroe Islands study found the effects of high maternal Hg exposures from consumption of even extraordinarily contaminated seafoods such as pilot whale meat, blubber, and liver were only associated with subtle diminishments in their children's subsequent performance assessments [67]. Children in the Faroes had cord blood Hg concentrations as high as 1 μM, a concentration which has been associated with adult Hg toxicity [71] and not coincidentally, ˜equimolar with the average concentration of Se in most body tissues. Maternal fish consumption was highly protective against the effects of Hg exposure in the Faroes [67], and ocean fish provided ˜80% of their dietary Se [61]. This is fortunate since otherwise fetal Se-status among those with high pilot whale meat consumption would have been grossly impaired. Since ocean fish are among the richest dietary sources of nutrients with important roles in brain health and development, including Se, long-chain omega-3 fatty acids, and vitamin D, it is not surprising that increased maternal fish consumption correspond with improved fetal outcomes.

The U.S. Environmental Protection Agency and the U.S. Food and Drug Administration advisory regarding fish consumption for children and pregnant women [72] includes a chart of > 60 types of fish and shellfish that women and children are encouraged to eat up to 3 servings per week depending on species. Nearly 90% of fish eaten in the U.S. fall into this "best choices" category, and these recommendations are consistent with positive HBV's based on their high Se contents relative to Hg. The advisory's "choices to avoid" category includes: shark, swordfish, king mackerel and tilefish from the Gulf of Mexico, orange roughy, marlin, and bigeye tuna. The present study found that mako sharks and large swordfish have negative HBVs which generally coincides with the Hg-based criteria used to establish EPA/FDA categories. However, thresher sharks had uniformly positive HBV's. Considering there are more than 400 shark species and the advisory does not differentiate among them, more work should be done to assess the HBV's of commonly consumed shark varieties to segregate those with positive vs. negative HBV's. The HBV's of king mackerel, tilefish, and orange roughy have not been assessed, but considering their high Hg contents, maternal consumption of these varieties should be limited until assessments have been performed. In contrast to the advisory, we find the uniformly positive HBV's of bigeye tuna (HBV = 11.5 $\pm$ 3.8; see Table 2), and marlin (HBV = 11.5 $\pm$ 4.2 for blue marlin, 8.0 $\pm$ 3.2 for striped marlin; unpublished data), indicate their Hg contents are unlikely to be problematic and should not be a basis for inclusion in the "choices to avoid" category. Criteria based on fish Hg contents alone lack merit because they include only half the information required to differentiate Hg-exposure risks from nutritional benefits of seafood consumption.

It is important to point out that the amount of Se in the food web of freshwater bodies and estuaries can vary depending on Se availability in their watersheds. Thus, the CH_3Hg and Se levels in freshwater fish can differ considerably. Bioaccumulation of CH_3Hg in piscivorous freshwater fish is inversely related to Se bioavailability. [73,74–80] Fish from regions with poor soil Se levels (e.g., in Finland, Canada, South America) will tend to have increased CH_3Hg contents and lower HBV's. Since Se-status of remote populations in Se-poor regions is likely to be low, Hg exposure risks may be exacerbated in subsistence fish consumers. [60] The current EPA freshwater fish advisories are based solely on Hg levels and vary from state to state. However, like ocean fish, freshwater fish from most North American watersheds generally contain significantly more Se than Hg [81,82] and therefore have positive HBV's. This suggests that many water bodies currently listed as "impaired" based on fish Hg contents may need to be reevaluated. In contrast, the low Se levels which tend to be common in high-Hg freshwater fish from Se-poor watersheds may indicate accentuated Hg-related risks which are currently being overlooked. This is especially true of subsistence fish consumers whose locally-sourced foods may also be Se poor would be at greatest risk from eating fish with negative HBVs. Therefore, freshwater fish and other foods which may contain high concentrations of Hg and other metallic or organic electrophiles should be evaluated using HBV criteria to identify populations that are increased at-risk and enhance the reliability of future risk assessments.

5. Conclusions

It is more rational to base maternal seafood consumption advice on the outcomes of studies of ocean fish eating populations than on the effects of exposures to toxicants which were predominantly from eating pilot whale meat, organs, and blubber. As previously observed with the majority of other ocean fish species, this study found skipjack tuna has a uniformly positive HBV that indicates it is safe and beneficial to eat. Since the HBV's of bigeye tuna, marlin, and thresher shark were also uniformly positive, they should not be considered "choices to avoid". While the negative HBV of mako sharks and large swordfish superficially aligns with the FDA/EPA "choices to avoid" category, suggesting avoidance may be inappropriate since most consumers fail to distinguish between different types of fish and many over-react to food-safety warnings. Therefore, to minimize risk of harm while optimizing fetal/infant neurodevelopment, the most prudent advice is to encourage maternal consumption of a variety of ocean fish with emphasis on those with positive HBV's.

Conflict of interest and funding disclosure

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