RECENT ADVANCES IN OUR KNOWLEDGE OF MERCURY AND SELENIUM ON HEALTH

Lemire, M. and Mergler, D.

2009 National Forum on Contaminants in Fish
Portland, Oregon
November 2-5, 2009

What is selenium ?

An essential trace element and a well known antioxidant

- Component of 25 selenoproteins in human:
  - Glutatione peroxidase (GPx)
  - Thioredoxin reductase
  - Selenoprotein P (SelP)

- Selenoenzymes are involved in:
  - Antioxidant and redox reactions
  - Thyroid hormone metabolism
  - Se transport

What are the sources of selenium?

Se in food and others

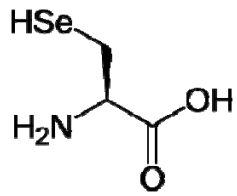
- Fish: Marine > Freshwater ML2
- Marine mammal and seafood
- Some plant species: Brazil nuts
- Organs, beef, chicken, eggs

- Occupation
- Drinking water

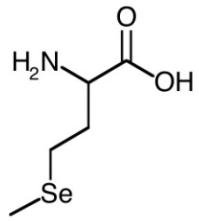
- Supplements

Se compounds

- Organic



SeCys



SeMet

- Inorganic

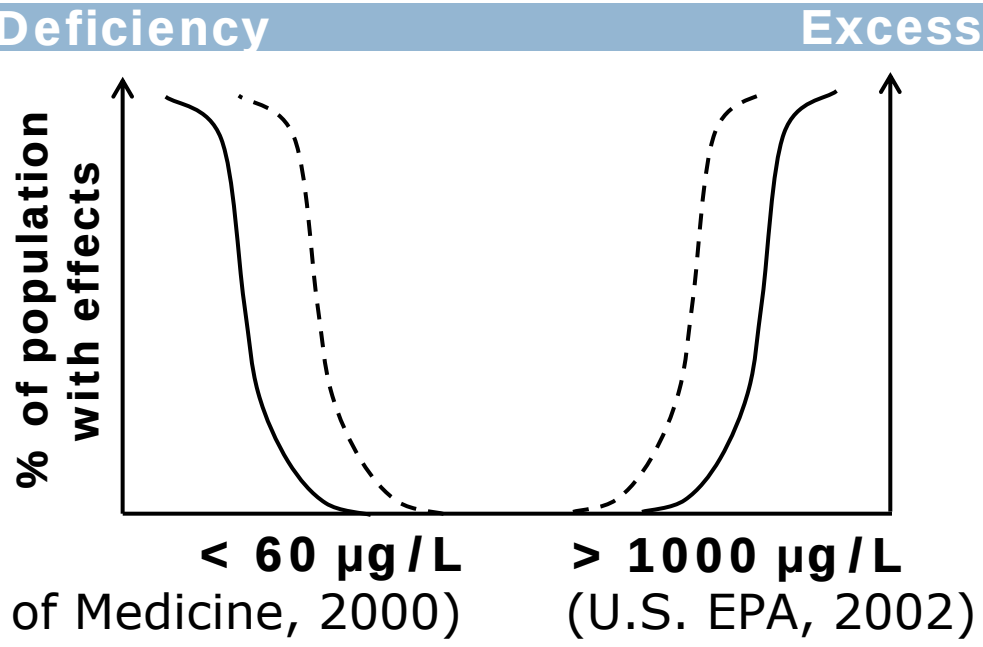
- Inorganic and organic ?

Slide 3

ML2 Marine > Freshwater: Large marine predators contain in general more SE than smaller freshwater fish, although it depends a lot of the trophic position and the overall Se content in the ecosystem

Mélanie Lemire, 10/12/2009

Selenium: Deficiency versus Excess



- Cancer
- Thyroid hormones perturbations
- Cardiovascular diseases
- Reproduction disorders

- Alterations in keratin structure
- Gastrointestinal problems
- Incidence of type 2 diabetes
- Possible neurological disorders
- Higher prevalence of cataracts

Se effects on Hg toxicity

In fish:

- Hg-Se covalent binding in fish would reduce Hg bioavailability and related-toxicity for human

Experimental studies :

- Proposed mechanisms:
  - Selenoproteins can offset Hg-mediated oxidative stress
  - Se-Hg complex can reduce Hg bioavailability to target organs
  - Se may be involved in demethylation of MeHg
  - Se intake restores selenoproteins inactivated by Hg

Human studies:

- Inconsistent epidemiological data

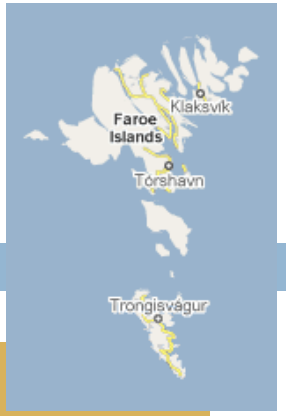
Human studies

Faroe Islands, Denmark

Nunavik, Canada

Amazon, Brazil

Faroe Islands – prenatal exposure



Steuerwald et al. (2000)

Choi et al. (2008)

- N = 182
- Cord blood Se: 103 µg/L (93 – 112 µg/L)
- Cord blood Hg: 20 µg/L (12 – 40 µg/L)

- Hg : **decrease** in the neurologic optimality score in neonates of 2 weeks of age
- Hg : **decrease** in neurobehavioral performances at 7 years of age

No effect of Se on Hg neurodevelopmental toxicity

Nunavik – Inuit preschool children

Després et al. (2005)

Saint-Amour et al. (2006)

- N = 110
- Blood Se: 329 µg/L (157 – 2566 µg/L)
- Blood Hg: 6 µg/L (0.2 – 38 µgL)

- Hg = **increased** hand tremor
- No effect of Se on motor functions

- Hg = **shorter** visual evoked potential latency (N75 and P100 at 95% and 30% contrast)
- Se = **longer** visual evoked potential latency (N75 and P100 at 95% and 30% contrast)
- No significant Se*Hg interactions

Nunavik - Inuit adults

Valera et al (2009)

- N = 132
- B-Se: 292 µg/L (118 - 3553 µg/L)
- B-Hg: 10 µg/L (0.2 - 241 µg/L)

Selenium and blood pressure (BP):

- Taking into account co-variables (B-Hg and n-3 fatty acids), B-Se is negatively associated to:
  - systemic BP: β = -2.8, P=0.03
  - diastolic BP: β = -1.7, P=0.07

- **No interaction**: Mercury and n-3 fatty acids did not show a modifier effect on the relationship between selenium and BP parameters

Brazilian Amazon

2006 study
Health effects of selenium in the Lower Tapajós region

- Cross-sectional study
- 12 communities
- 450 participants from 15 to 87 years

- Examine the levels of Se in local food and water
- Examine the relations between biomarkers of Se and:
  - Sentinel signs and symptoms of Se toxicity
  - Oculo-visual health
  - Motor and sensory functions

Levels of selenium in local foods

		Median	Range
Low	Drinking water (µg/L)	0.05	0.05 – 1.4
	Fruits and vegetables (µg/g)	< 0.1	
Medium	Kale, sweet potato, rice and *pupunha* (µg/g)	0.1	0.01 – 0.6
High	Chicken, game meat, eggs, freshwater fish, meat (µg/g)	0.5	0.05 – 1.4
Very high	Brazil nut (µg/g) *Bertholletia excelsa*	13.9	0.4 – 158.4

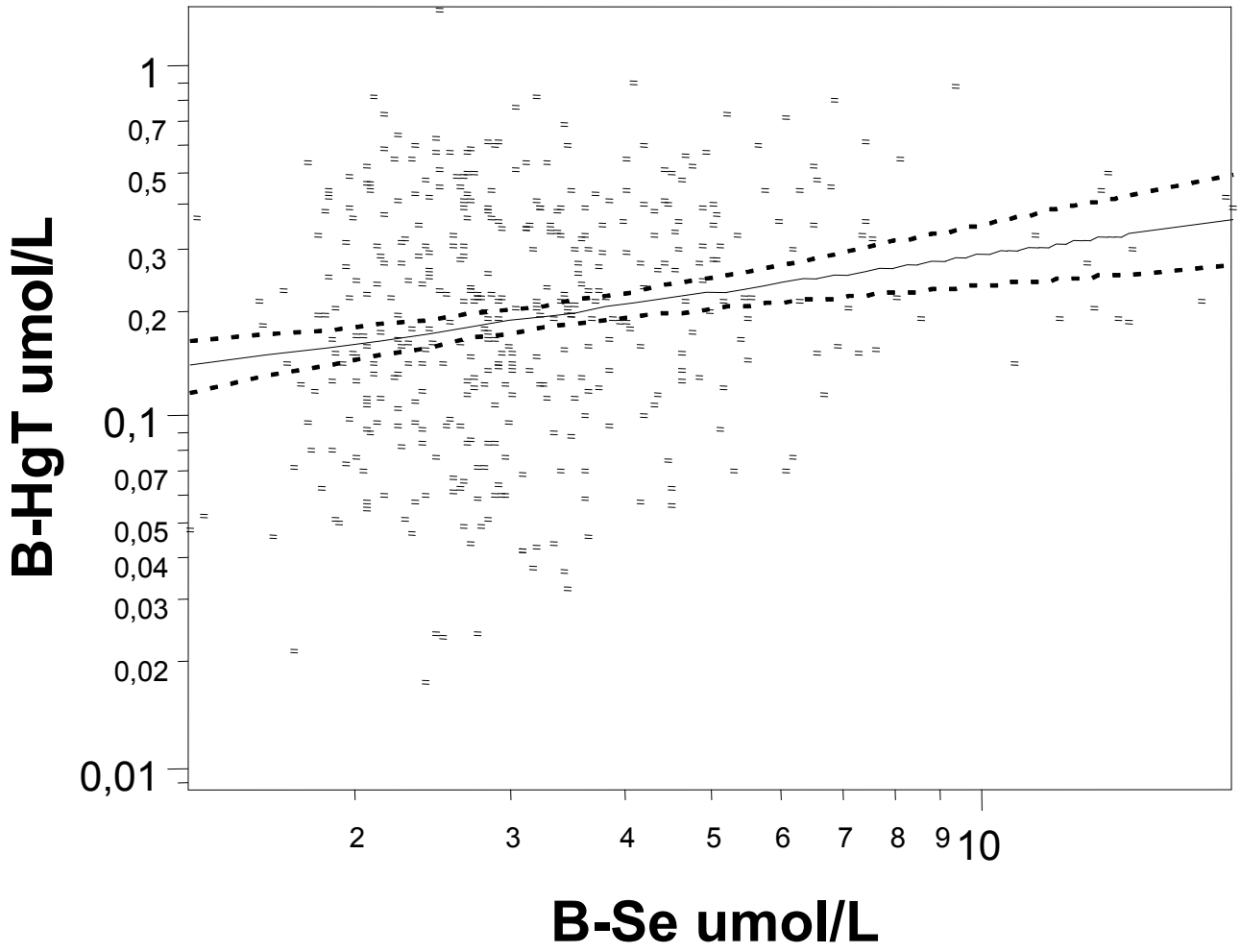
Biomarkers of Se and Hg

- Blood Se (B-Se): 228 µg/L (103 – 1500 µg/L)
- Plasma Se (P-Se): 135 µg/L (54 – 913 µg/L)
  - Highly related to Brazil nut consumption
  - Not related to fish consumption

- Blood Hg (B-Hg): 42.5 µg/L (1.7 – 288.9 µg/L)
  - Highly related to fish consumption

- Although B-Se and P-Se surpassed concentrations considered toxic:
  - **no signs or symptoms of Se toxicity were associated with these biomarkers of Se status**

Se – Hg ratio



Mean Hg/Se ratio :

0.08 ± 0.07

(0.002 – 0.58)

B-Hg µmol/L = 0.22 + 0.01*B-Se µmol/L (P = 0.005)

Motor performance

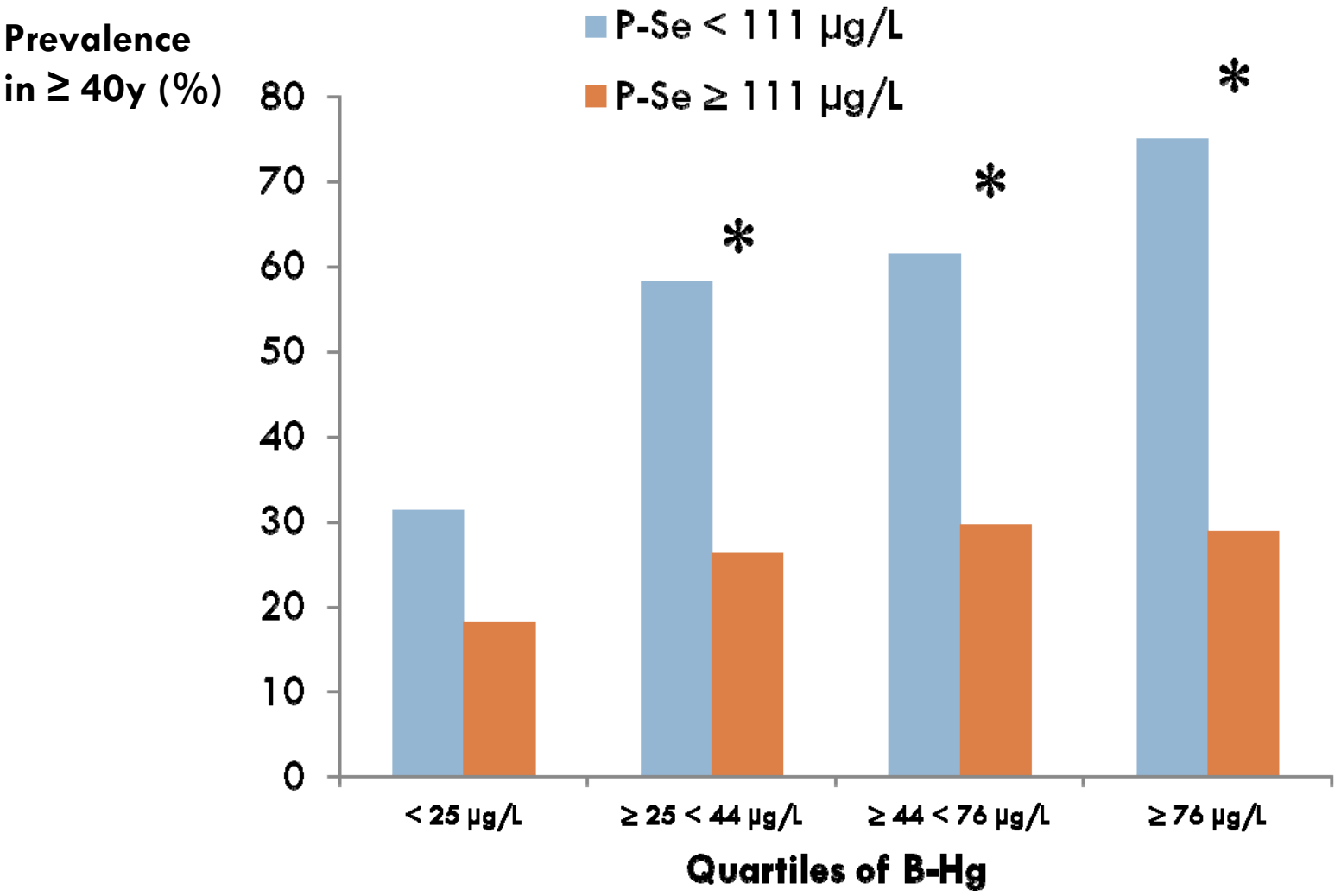
Multiple regression models (including B-Hg and co-variables)

Outcome	B-Se	P-Se	H-Se	U-Se
Motor coordination	↑*	↑**	ns	ns
Manual dexterity	ns	↑ *	ns	↑ †
Fine motor movement	↑*	↑ *	ns	ns
Grip strength	↑ †	↑ *	ns	ns

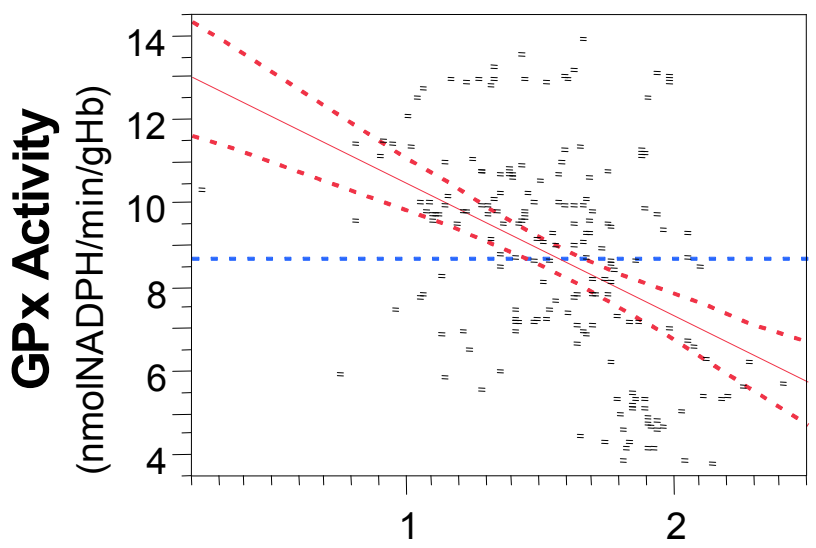
† : p < 0.10 * : p < 0.05 ** : p < 0.01 *** : p < 0.0001

- **No significant Se*Hg interactions**

Ocular health: 32.6% age-related cataracts in adults of 40y and more

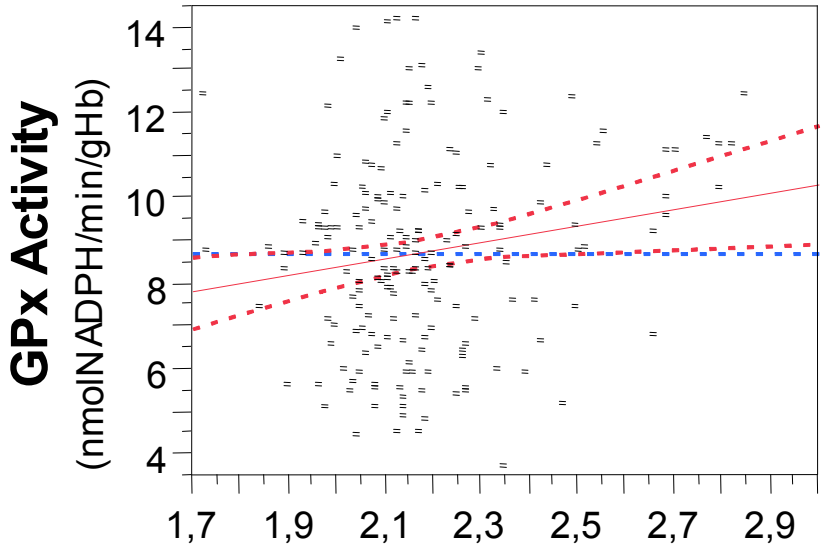


GPx activity in erythrocytes



Log B-Hg (µg/L) P<0.0001

(Grotto et al, in press)



Log P-Se (µg/L) P=0.02

- N = 183
- Not related to B-Se levels
- **No P-Se * B-Hg interaction on GPx activity**

Conclusions (I)

- **High Se status:** marine fish/mammals and Brazil nut eating populations

- **None of the classic toxic effects of selenium reported in the literature was observed in the Amazon:**
  - NOAEL : based on China' studies reporting Se chronic toxicity where Se exposure is both inorganic Se (mineral coal) and organic Se (food)
  - Organic forms of Se in Amazonian diet

- **P-Se = biomarker best related to health outcomes**
  - In erythrocytes proteins, there is an important non-specific incorporation of SeMet, which is probably less bioavailable for selenoprotein synthesis

- **No statistical interactions between Se and Hg biomarkers and the health outcomes were observed**

Conclusion (II)

- **All of the human studies performed to date were on populations with high Hg and high Se**

- In populations highly exposed to Hg:
  - **Adequate, or even elevated, Se intake may be important** to:
    - offset toxic effects of Hg
    - maintain optimal Se antioxidant enzymes

  - **There may be less 'excess' of Se and consequently little or no Se toxicity**

Conclusion (III)

- The effects of **Se with respect to Hg toxicity are complex** and many factors may explain the inter-study differences:
  - Se sources and Se speciation
  - Biomarkers of Se status
  - Levels of Hg exposure
  - State of development (*in utero* vs adult)

- **More studies are needed to better understand the conditions under which Se intake from food affects health outcomes in populations with moderate Hg intake**

Rewiew of human studies

Study	Se sources	Biomarkers	Pop.	Hg effects	Se effects
Faroe	Marine mammals & fish	Normal cord B-Se High cord B-Hg	Neonates Children	↓ Neurobeha-vioral fonctions	None
Nunavik	Marine mammals & fish	Normal/High B-Se High B-Hg	Children	↑ Hand tremor	None
			Children	↓ VEP latency	↑ VEP latency
		Normal/High B-Se High B-Hg	Adults	↑ Blood Pressure	↓ Blood Pressure
Amazon	Brazil nuts & others	Normal/High B-Se High B-Hg	Adults	↑ Age-related cataract	↓ Age-related cataract
				↓ Motor functions	↑ Motor functions

CARUSO project
Lower Tapajós region

Slash and burn agriculture

Deforestation

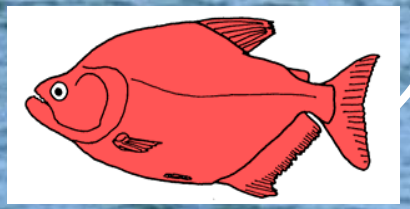
Soil erosion

Hg in water

MeHg

Health effects

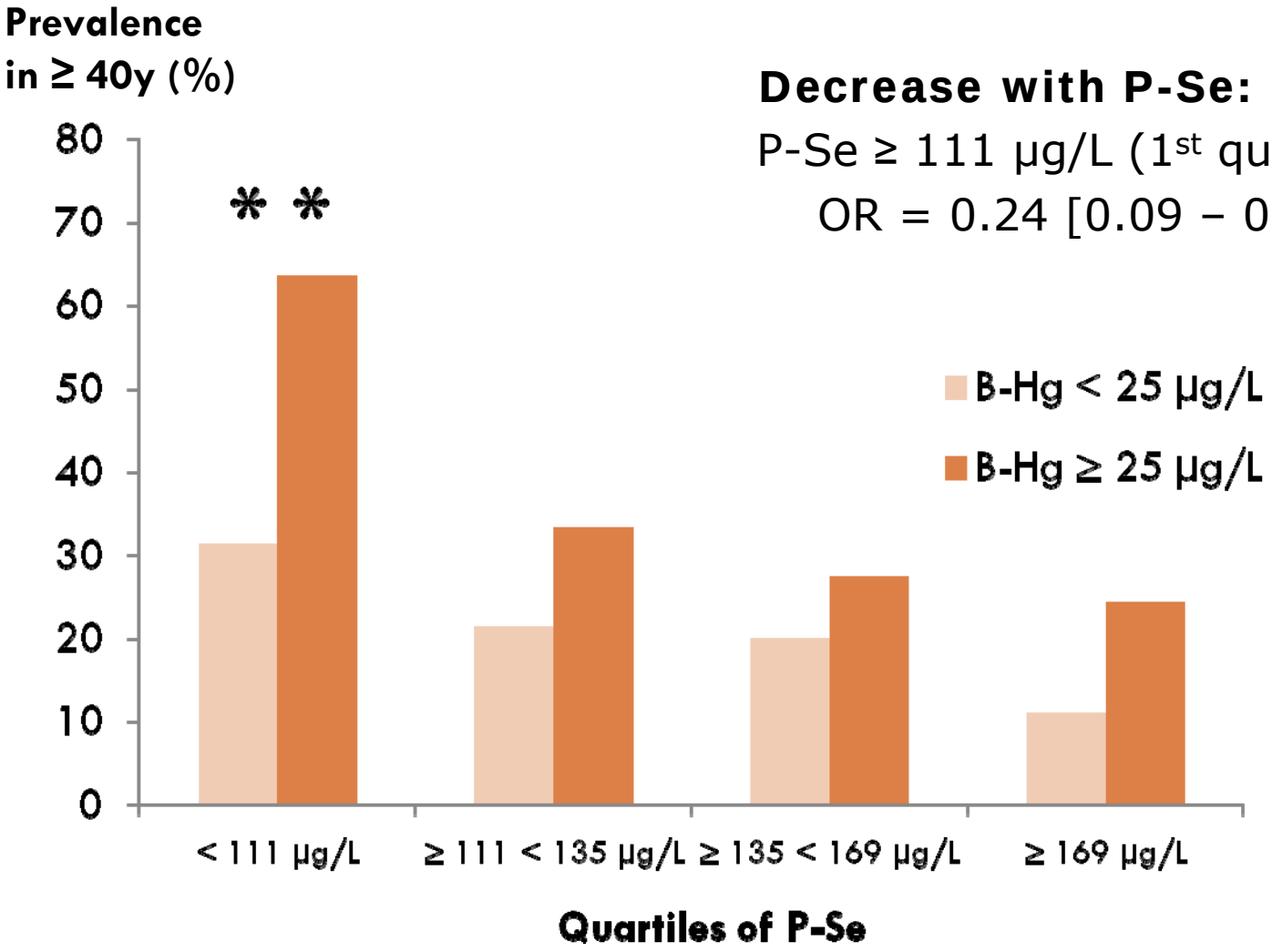
Human exposure



Bioaccumulation and biomagnification of MeHg

Faroe Islands

Plasma Se and age-related cataracts

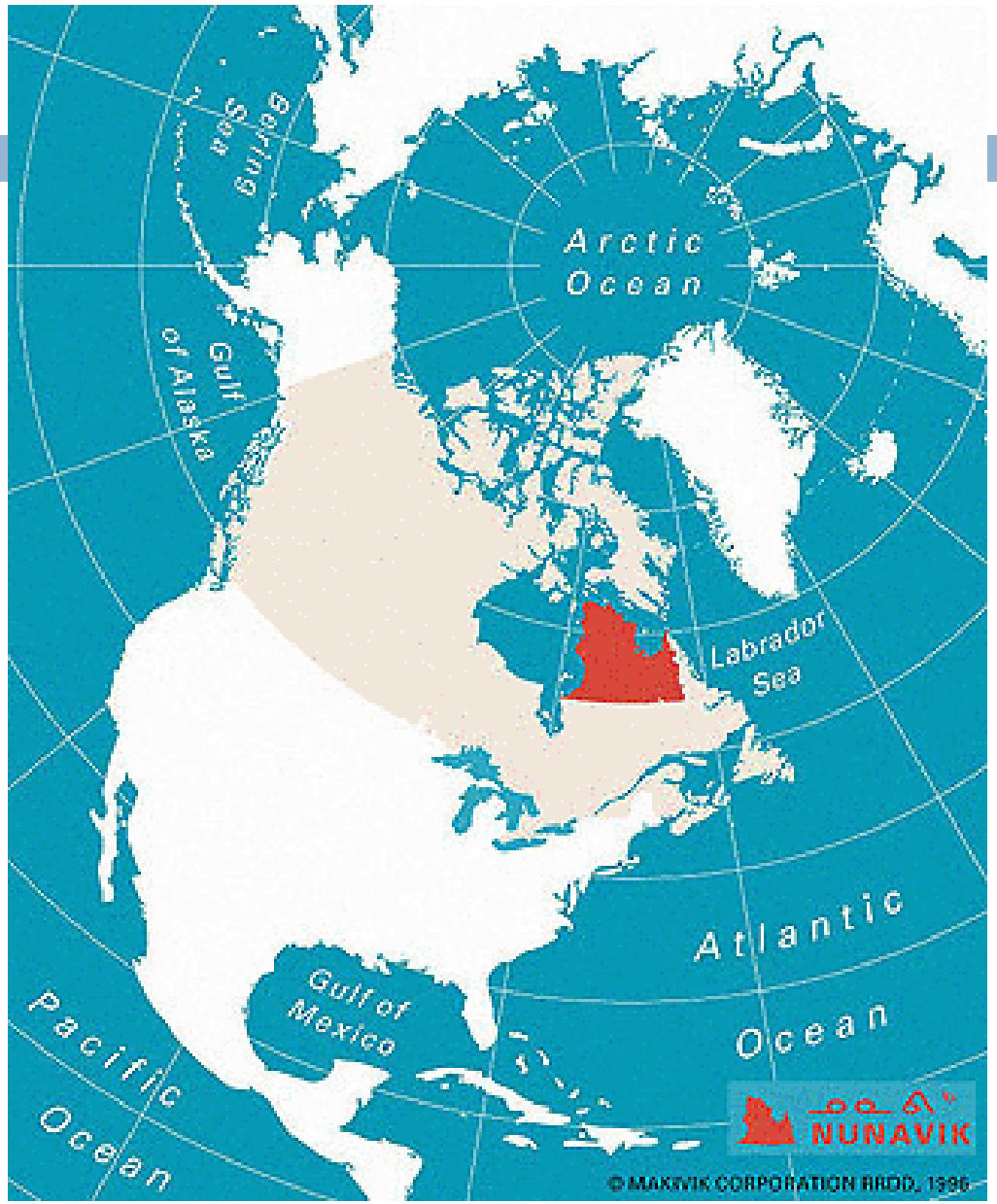


Decrease with P-Se:

P-Se ≥ 111 µg/L (1st quartile):

OR = 0.24 [0.09 – 0.61] **

Nunavik


Bering Sea
Gulf of Alaska
Arctic Ocean
Labrador Sea
Atlantic Ocean
Gulf of Mexico
Pacific Ocean
NUNAVIK
© MAKIVIK CORPORATION BRDD, 1996