Mahidol University

Wisdom of the Land

Environmental Exposure to Heavy Metals and Cognitive Function in Thai Elderly Population

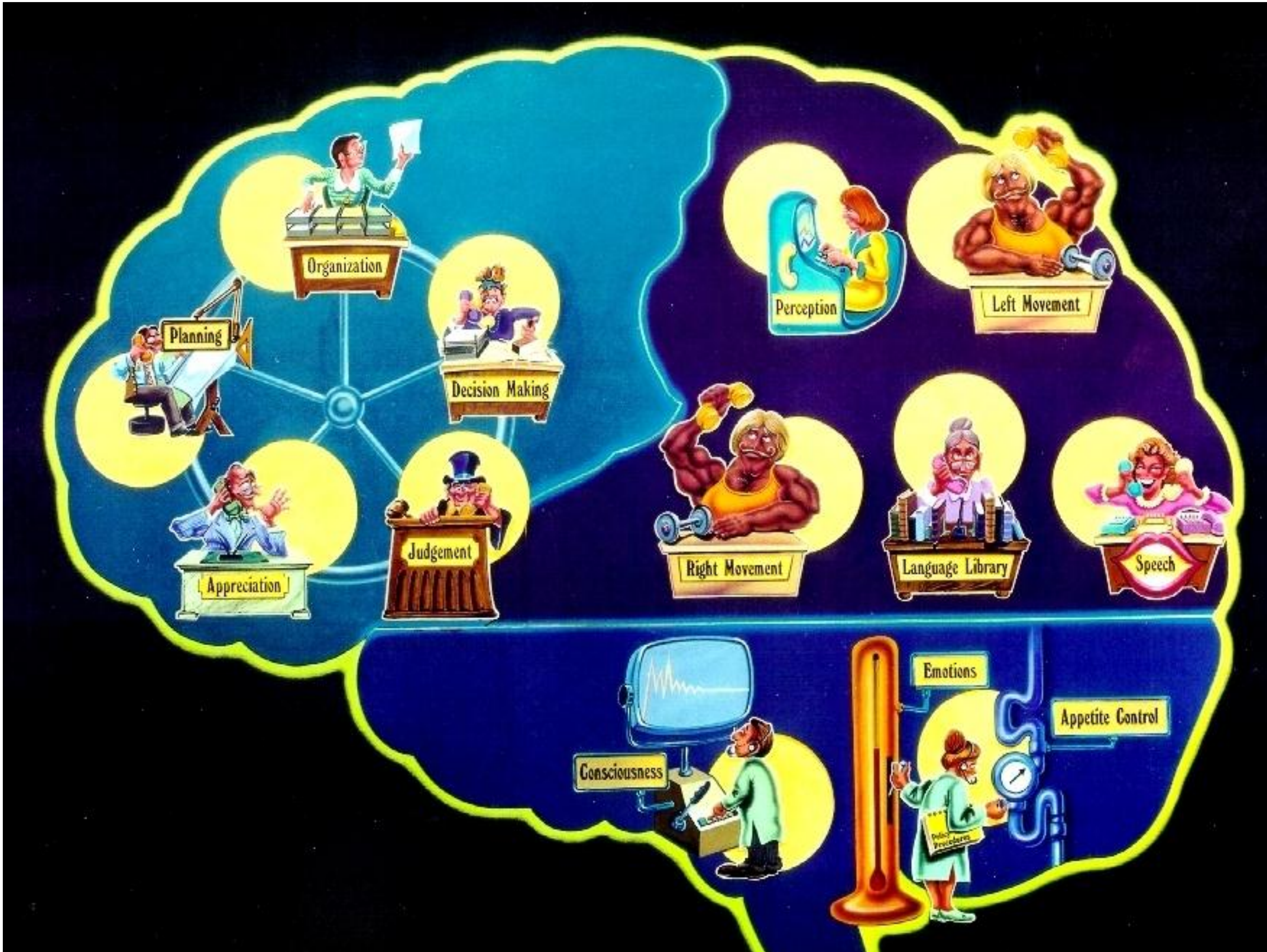
Jintana Sirivarasai, Ph.D

Division of Clinical Pharmacology and Toxicology
Department of Medicine
Faculty of Medicine Ramathibodi Hospital

December 14, 2012

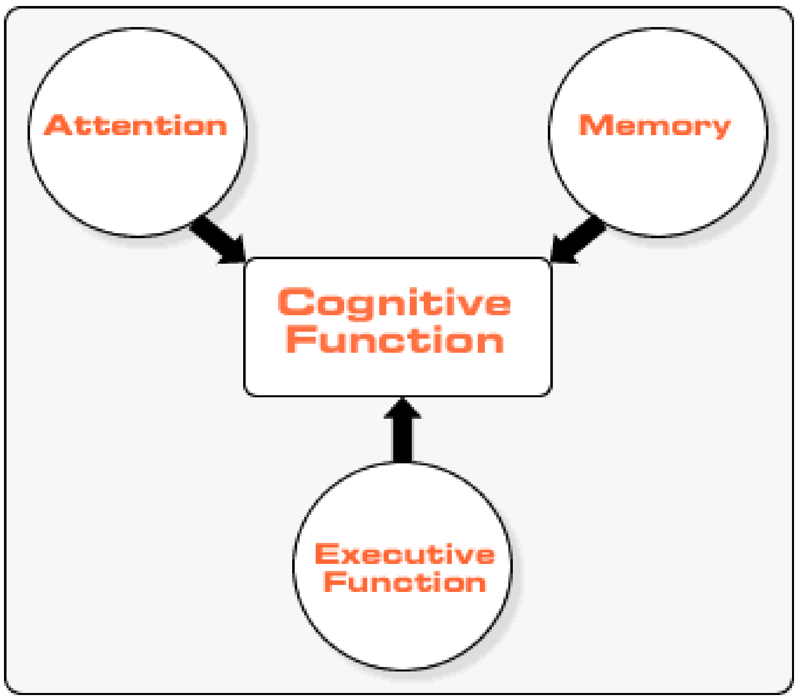
EGAT 1/5 : 2012

- Lead (Pb)
- Cadmium (Cd)
- Mercury (Hg)


Organization
Planning
Decision Making
Appreciation
Judgement
Perception
Left Movement
Right Movement
Language Library
Speech
Emotions
Appetite Control
Consciousness

MMSE Test

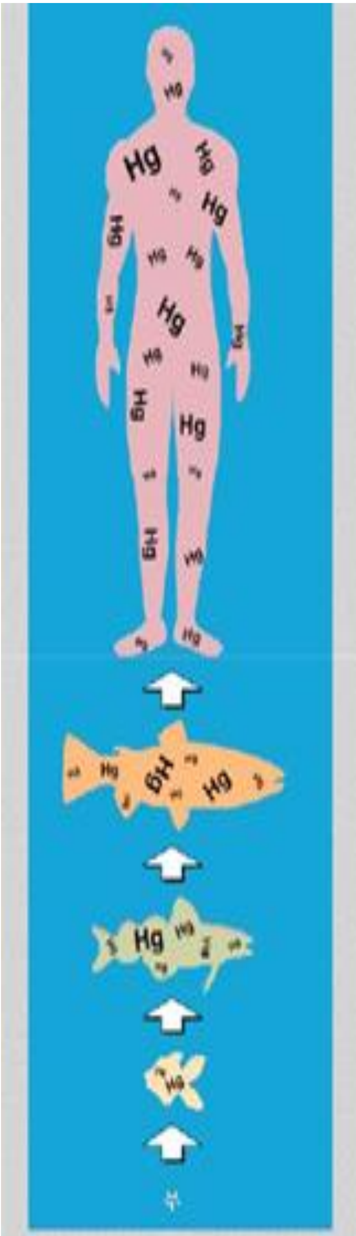
- Orientation for time (total score : 5)
- Orientation for place (total score : 5)
- Registration (total score : 3)
- Attention/calculation (total score : 5)
- Recall (total score : 3)
- Naming (total score : 2)
- Repetition (total score : 1)
- Verbal command (total score : 3)
- Written command (total score : 1)
- Writing (total score : 1)
- Visuoconstrution (total score : 1)

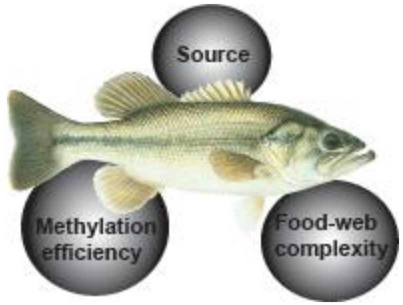


First study of heavy metals (Cd, Pb, and Hg with ICPMS) and cognitive function in Thai elderly population

Inductively coupled plasma mass spectrometry (ICP-MS)

Mercury (Hg)


Hg


Source
Methylation efficiency
Food-web complexity

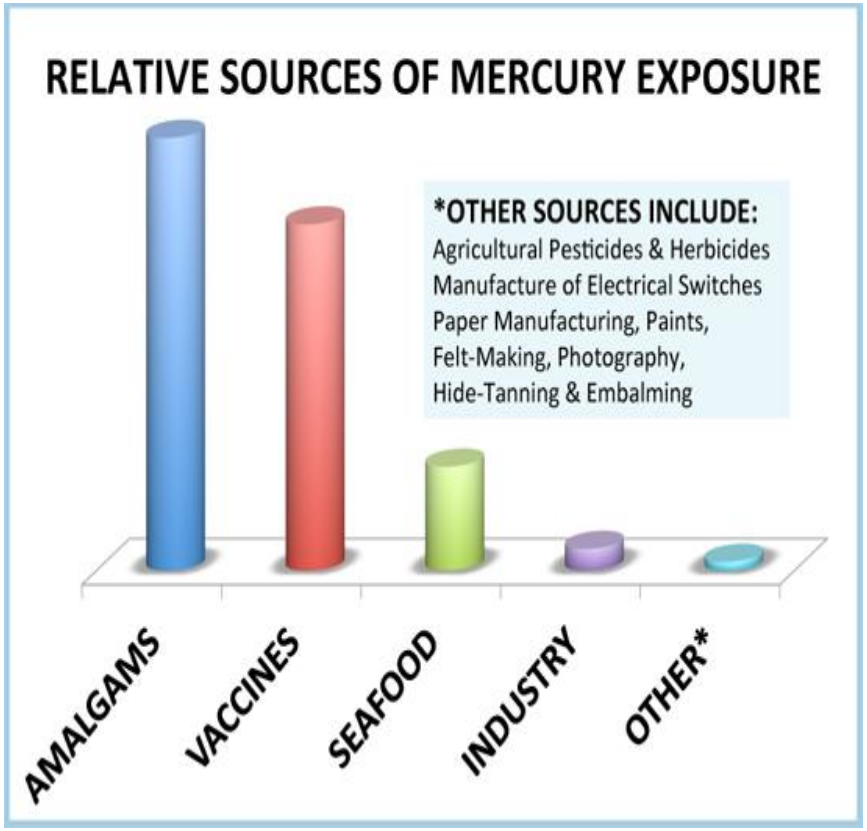

VACCINE
DEATHS & AUTISM
2007
1975

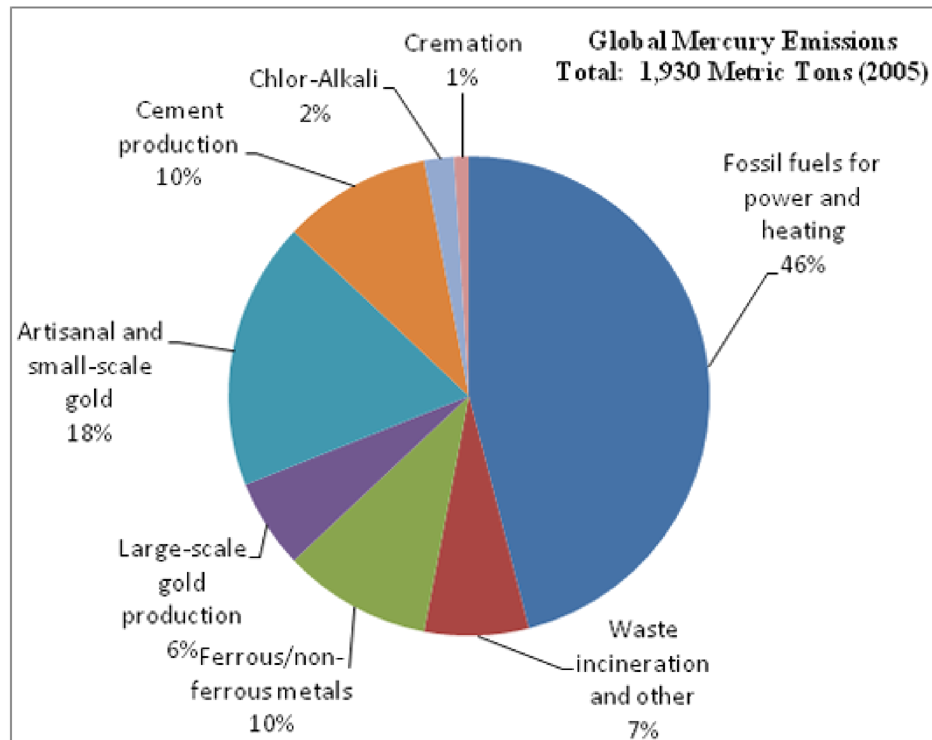

T-8784
SIGMA
Thimerosal
(Mercury-[(o-carb
SigmaUltra
Minimum 97% (H
Very toxic
Sehr giftig
Tres toxique
Muy toxico
Molto tossico
Zeer vergiftig
Light sensitive
Store at room temperature

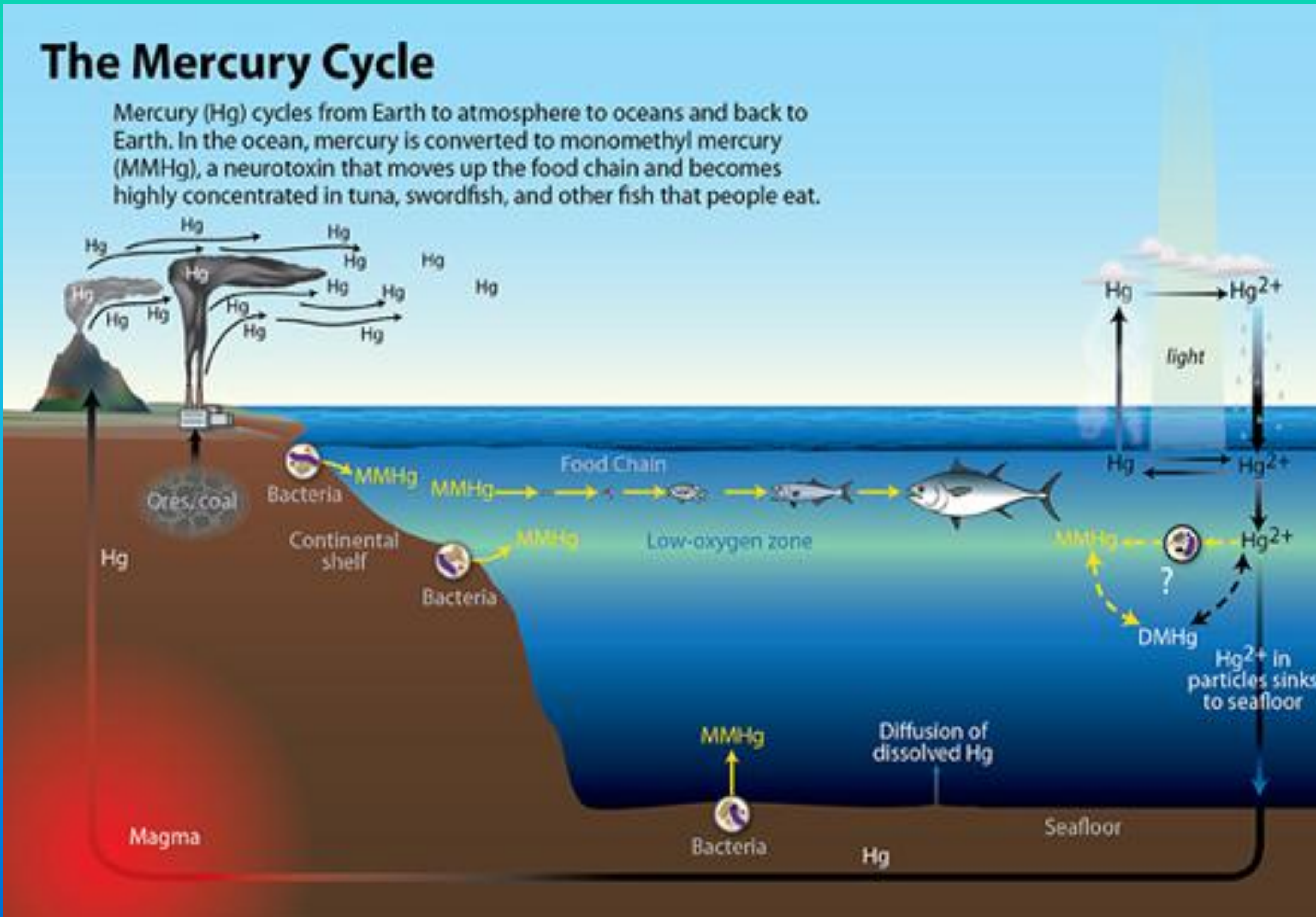

WALMART
Swordfish
Women of childbearing age and children should not eat
HIGH MERCURY!
.976 Parts Per Million
Shouldn't danger be advertised as prominently as discounts?


เครื่องสำอางที่ตรวจพบสารปรอท
LIVE
VOICE NEWS
VOICE TV

	Methylmercury	Elemental Mercury	Inorganic Mercury
Sources	Fish, poultry, pesticides	Dental amalgams, fossil fuels, old latex paint, thermometers, incinerators, occupational	Demethylation of methylmercury by intestinal microflora; biological oxidation of elemental mercury
Absorption	95–100 percent in intestinal tract; 100 percent of inhaled vapor	75–85 percent of vapor absorbed	7–15 percent of ingested dose absorbed; 2–3 percent of dermal dose absorbed in animals
Distribution	Lipophilic, distributed throughout body; readily crosses blood-brain barrier and placental barrier; accumulates in brain, kidney	Lipophilic, distributed throughout body; crosses blood-brain and placental barriers; accumulates in brain, kidney	Does not cross blood-brain or placental barrier; found in brain of neonates; accumulates in kidney
Metabolism	Cysteine complex necessary for intracellular absorption; slowly demethylated to inorganic mercury in brain by tissue macrophages, fetal liver, and free radicals	Oxidized intracellularly to inorganic mercury by catalase and hydrogen peroxide	Methylated by intestinal microflora; binds and induces metallothionein biosynthesis
Excretion	90 percent in bile,feces; 10 percent in urine	Urine, feces, sweat and saliva	Urine, bile, feces, sweat, saliva
Cause of Toxicity	Demethylation to inorganic (divalent) mercury; free radical generation; binding to thiols in enzymes and structural proteins	Oxidation to inorganic (divalent) mercury	Binding to thiols in enzymes and structural proteins


RELATIVE SOURCES OF MERCURY EXPOSURE
*OTHER SOURCES INCLUDE:
Agricultural Pesticides & Herbicides
Manufacture of Electrical Switches
Paper Manufacturing, Paints,
Felt-Making, Photography,
Hide-Tanning & Embalming
AMALGAMS
VACCINES
SEAFOOD
INDUSTRY
OTHER*


Global Mercury Emissions
Total: 1,930 Metric Tons (2005)
Cremation 1%
Chlor-Alkali 2%
Cement production 10%
Fossil fuels for power and heating 46%
Artisanal and small-scale gold 18%
Large-scale gold production 6%
Ferrous/non-ferrous metals 10%
Waste incineration and other 7%


The Mercury Cycle
Mercury (Hg) cycles from Earth to atmosphere to oceans and back to Earth. In the ocean, mercury is converted to monomethyl mercury (MMHg), a neurotoxin that moves up the food chain and becomes highly concentrated in tuna, swordfish, and other fish that people eat.
Hg
Hg → Hg2+
light
Hg ⇄ Hg2+
Ores/coal
Bacteria
MMHg
MMHg
Food Chain
Continental shelf
MMHg
Bacteria
Low-oxygen zone
MMHg
Hg2+
?
DMHg
Hg2+ in particles sinks to seafloor
MMHg
Diffusion of dissolved Hg
Bacteria
Seafloor
Magma
Hg

2-3 MEALS PER WEEK FROM THIS LIST

OR

1 MEAL PER WEEK FROM THIS LIST

AVOID
EAT RARELY, IF AT ALL

Follow these guidelines to reduce exposure to mercury, PCBs, and other contaminants:

2-3 meals per week:

- Anchovies
- Butterfish (Silver pomfret)
- Catfish
- Clams
- Cod (Pacific) (Atlantic)
- Crab (blue, king, snow, (US, Canada) (Russia)
- Crab-Imitation
- Crayfish
- Flounder/Sole (Pacific) (Atlantic)
- Herring
- Mackerel (canned)
- Oysters
- Pollock/Fish sticks
- Salmon (fresh, canned):
  - Chinook (coastal, Alaska)
  - Chum
  - Coho
  - Farmed (Atlantic) *
  - Pink
  - Sockeye
- Sardines
- Scallops
- Shrimp (US) (Imported)
- Squid/Calamari
- Tilapia (US, Central America) (China, Taiwan)
- Trout
- Tuna (canned light)

1 meal per week:

- Black sea bass
- Chilean sea bass
- Chinook salmon (Puget Sound)
- Croaker (white, Pacific)
- Halibut (Pacific) (Atlantic)
- Lobster (US, Canada)
- Mahi mahi
- Monkfish
- Rockfish/Red snapper (trawl caught)
- Sablefish
- Tuna (canned white Albacore) (WA, OR, CA troll caught)

Fish Not On the List? Call DOH toll free at 1-877-485-7316 for information.

* **Farmed Salmon** health and environmental impacts are controversial. For more information, visit www.doh.wa.gov/fish/farmedsalmon.

Women who are or may become PREGNANT, NURSING MOTHERS, and CHILDREN should NOT eat these fish:

- Mackerel (King)
- Marlin
- Shark
- Swordfish
- Tilefish
- Tuna steak

Adult Meal Size = 8 oz. UNCOOKED
Child Meal Size = 4 oz. UNCOOKED

A seafood meal appropriate for your body size is about the size and thickness of your hand.

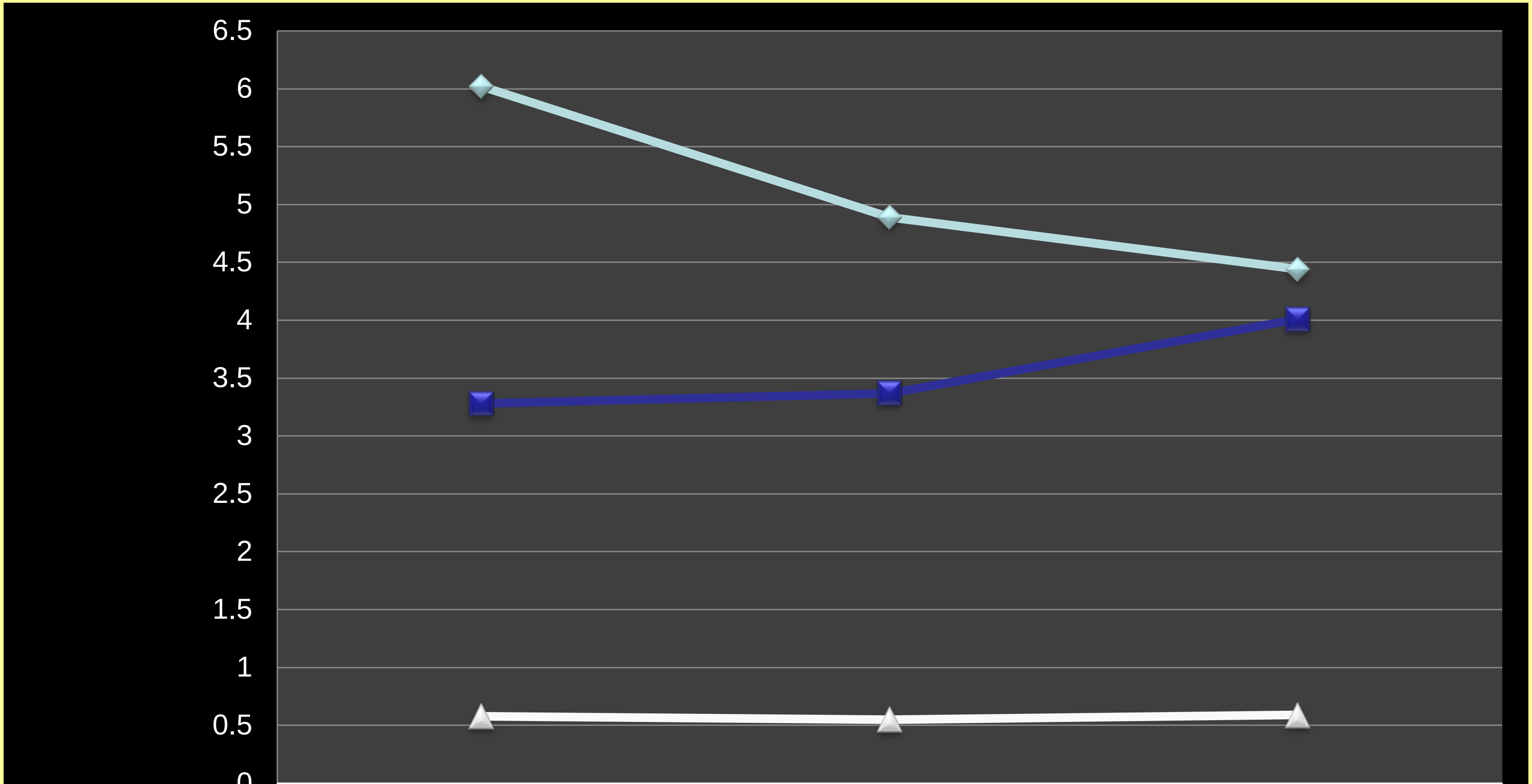
Figures based on a 160 lb. adult and an 80 lb. child. To personalize a meal size, add or subtract 1 oz. for every 20 lb. difference in body weight.

ORANGE TEXT indicates seafood choices that are over-fished or are harvested in environmentally harmful ways.

Mahidol University
Wisdom of the Land

Results

- Preliminary data : Limitation of data verifications
- Study population : 1609 cases, Male 72.4%
- Mean of age = 68.74 yr (60-82)



	60-69 years	70-79 years	> 79
Blood Hg (ug/L)	6.02	4.89	4.44
Blood Pb (ug/L)	3.28	3.37	4.01
Blood Cd (ug/L)	0.58	0.55	0.59

Fig 1. Means of blood Hg, Pb, and Cd levels classified by 3 age groups

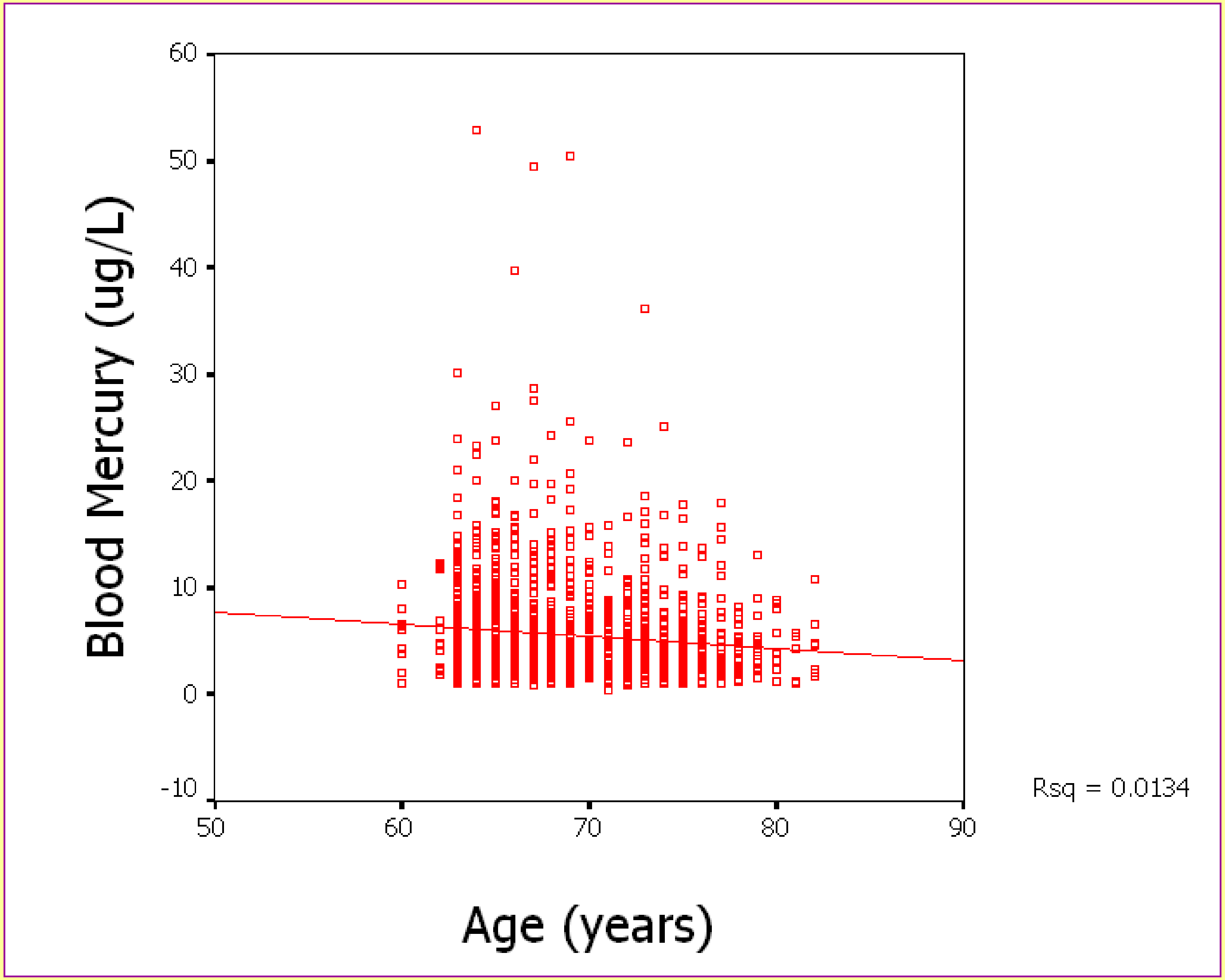


Fig 2. Association between blood Hg and age

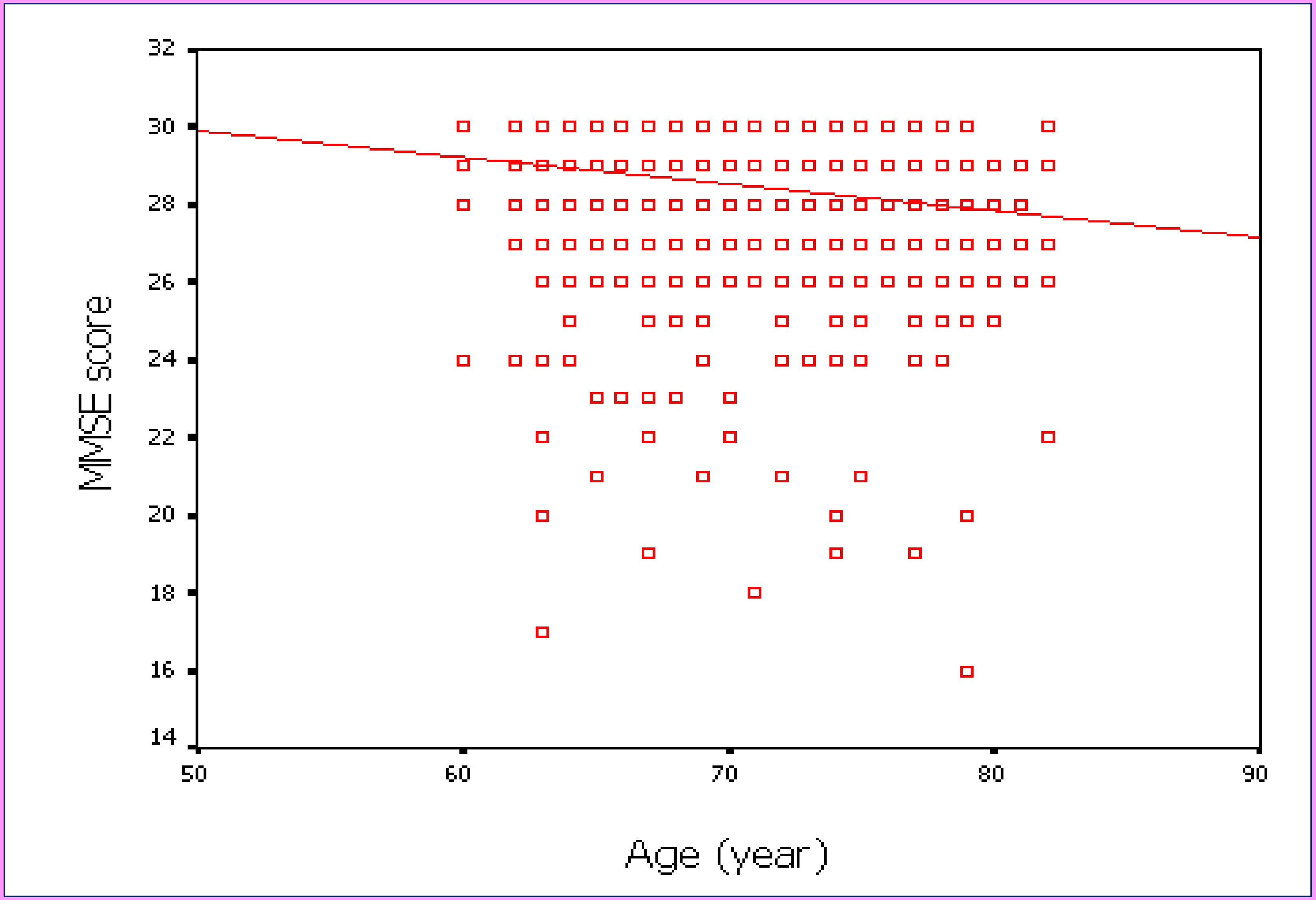


Fig 3. Association between MMSE score and age

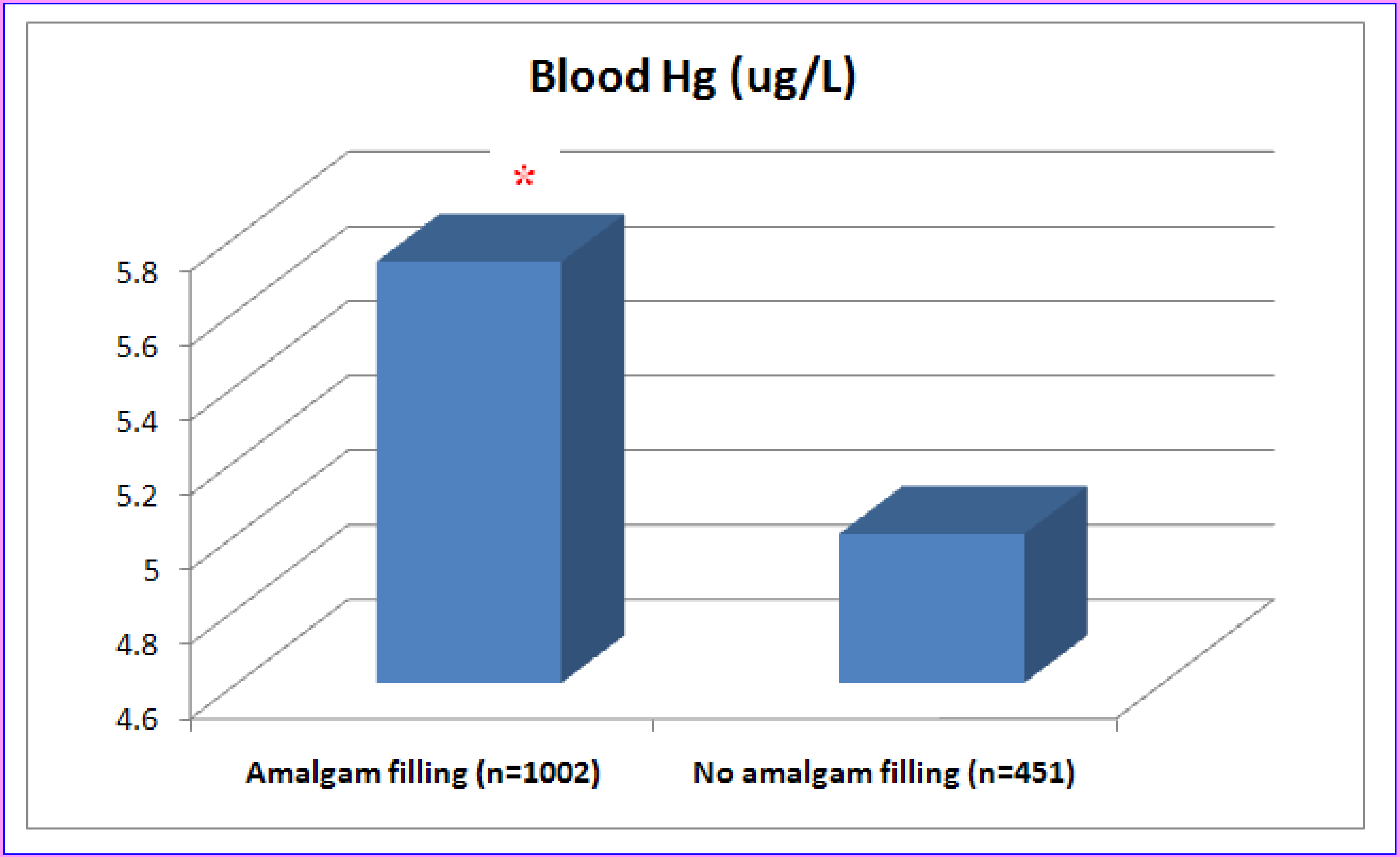
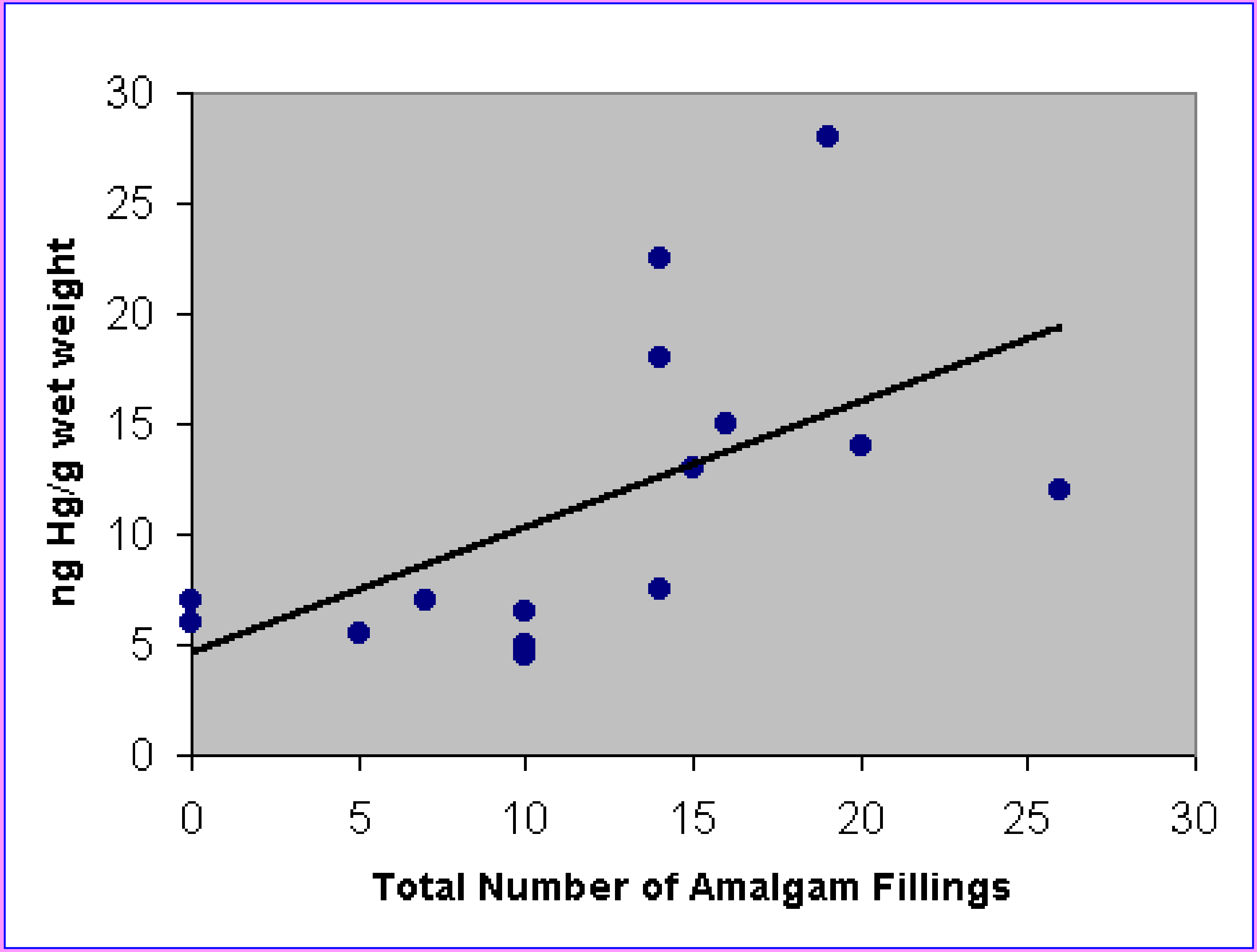


Fig 4. Blood Hg and amalgam filling

Mercury concentrations in the occipital cortex vs. number of amalgam fillings.



Nylander M, Friberg L, Lind B, & Kullman L: Mercury in the central nervous system correlated to dental amalgam fillings, Lakartidningen 1986 Feb 12;83(7):519-22

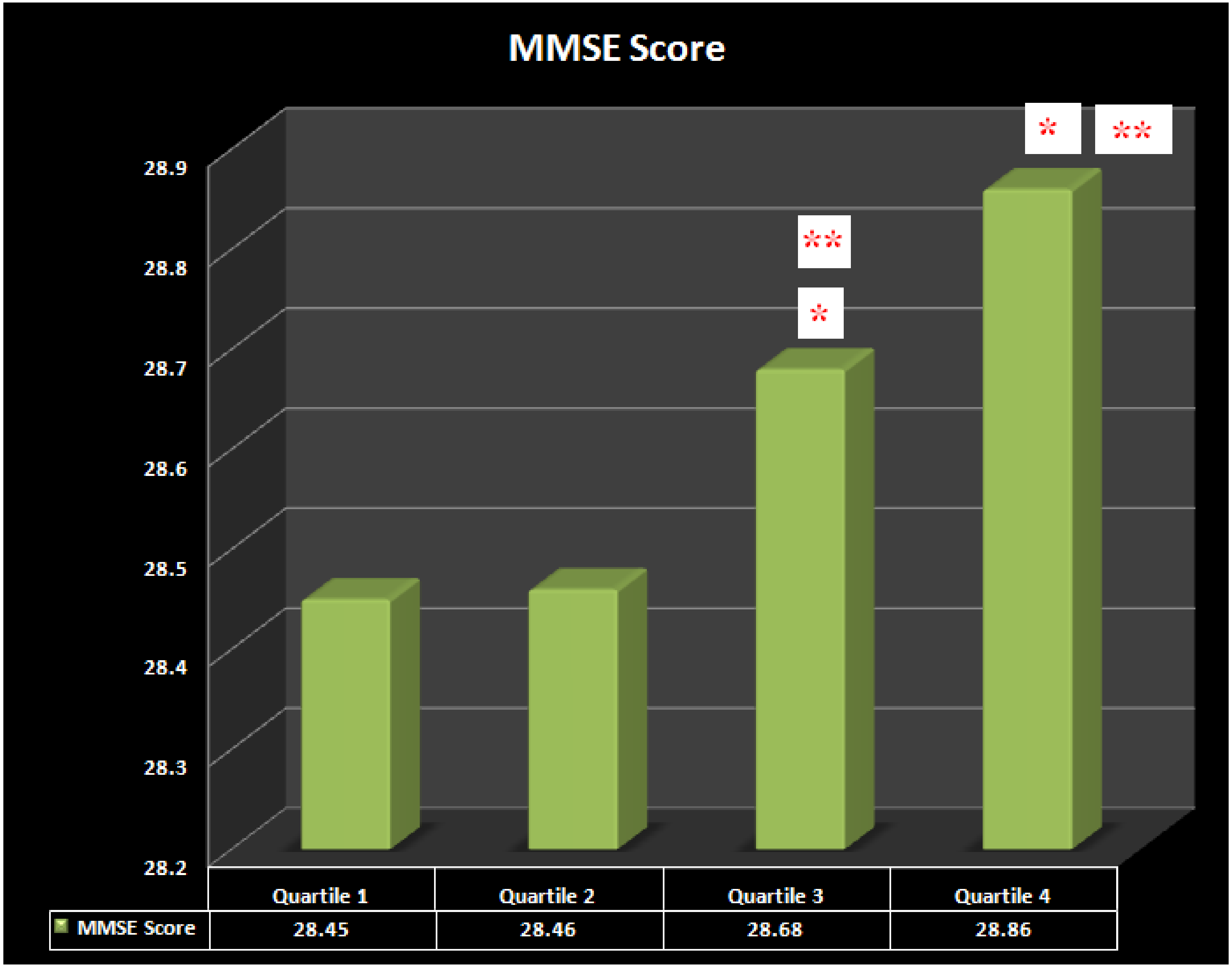


Fig 5. Blood Hg in each quartile and MMSE score

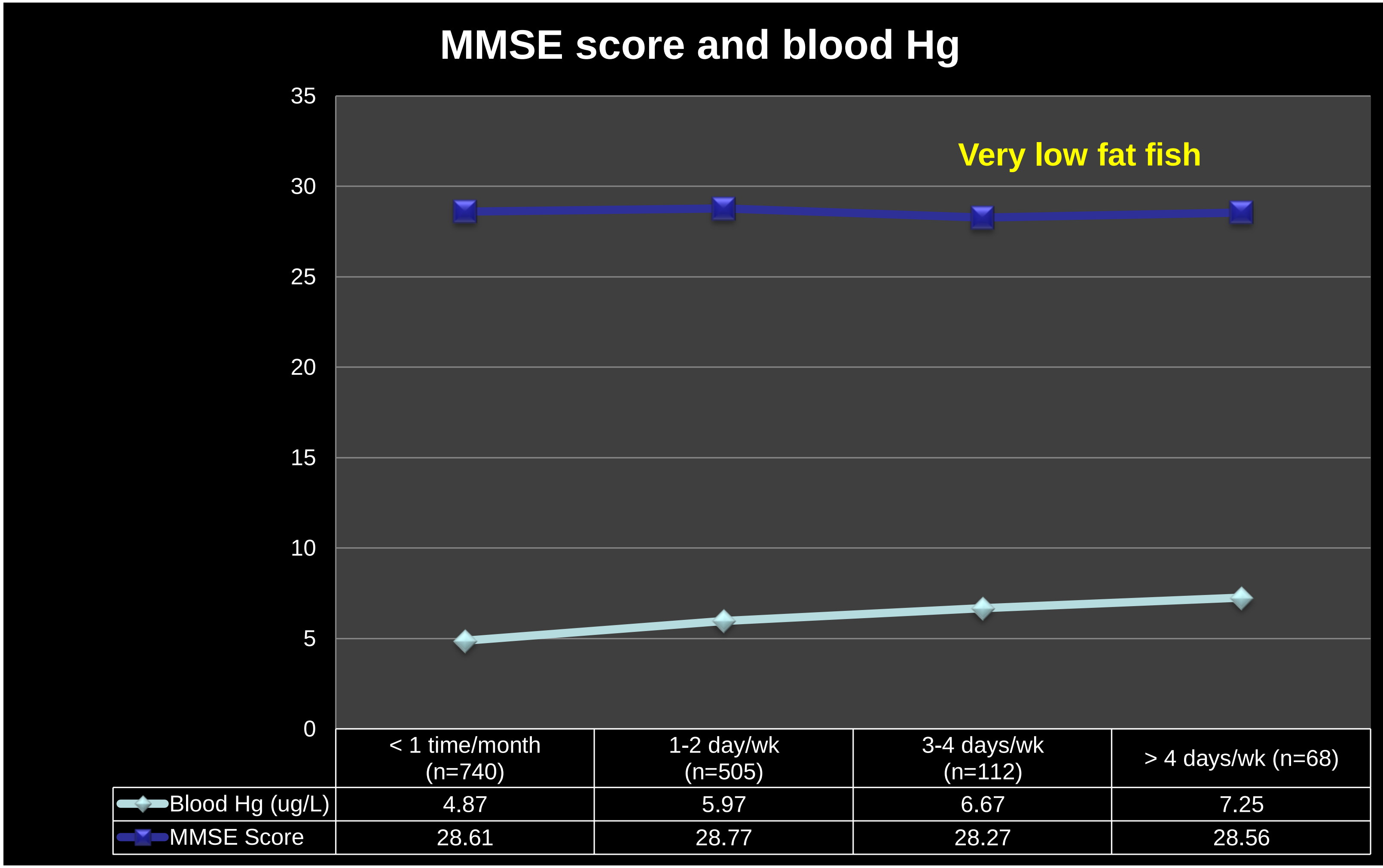
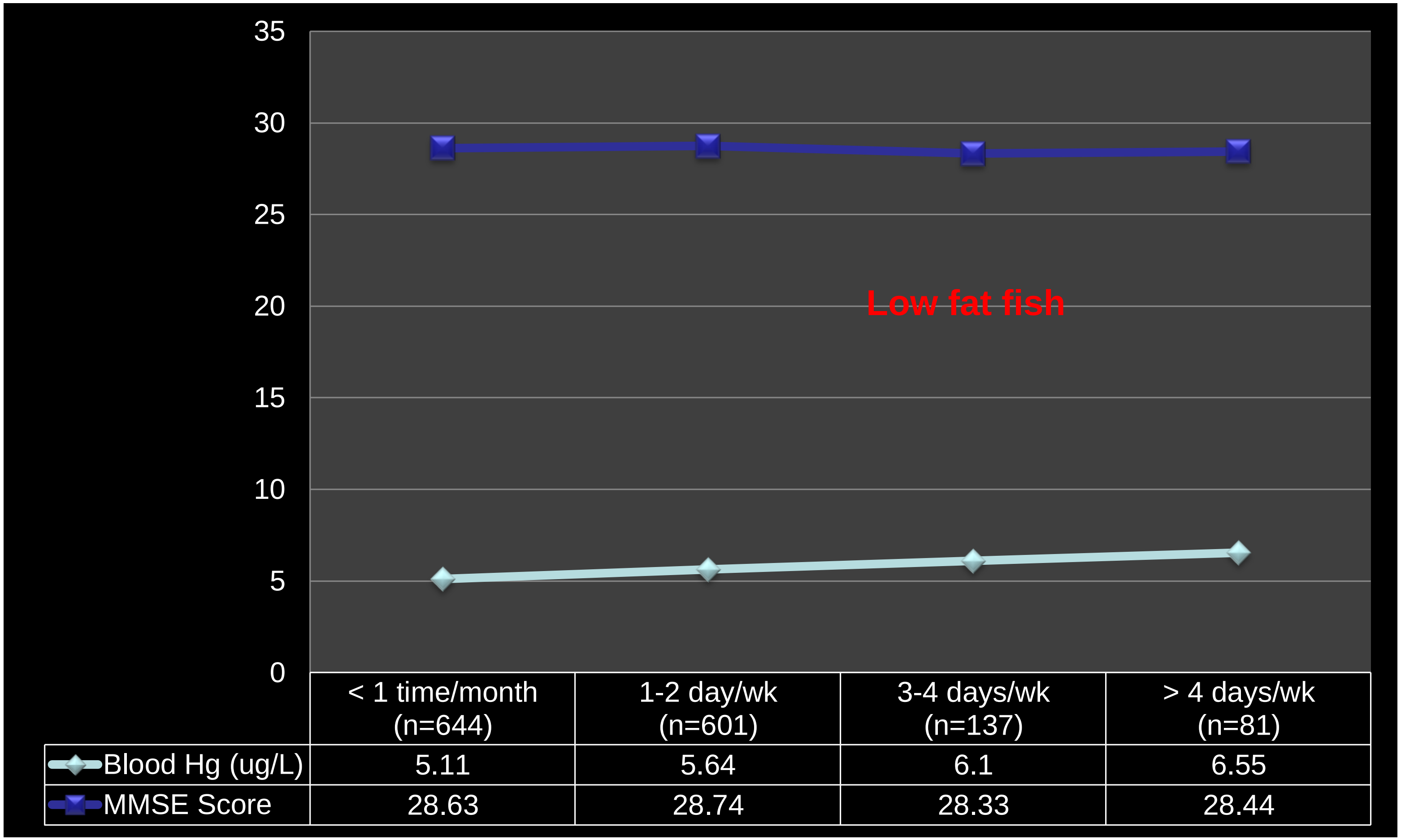


Fig 6. Blood Hg and MMSE score, classified by very low fat-fish intake



	< 1 time/month (n=644)	1-2 day/wk (n=601)	3-4 days/wk (n=137)	> 4 days/wk (n=81)
Blood Hg (ug/L)	5.11	5.64	6.1	6.55
MMSE Score	28.63	28.74	28.33	28.44

Fig 7. Blood Hg and MMSE score, classified by low fat-fish intake

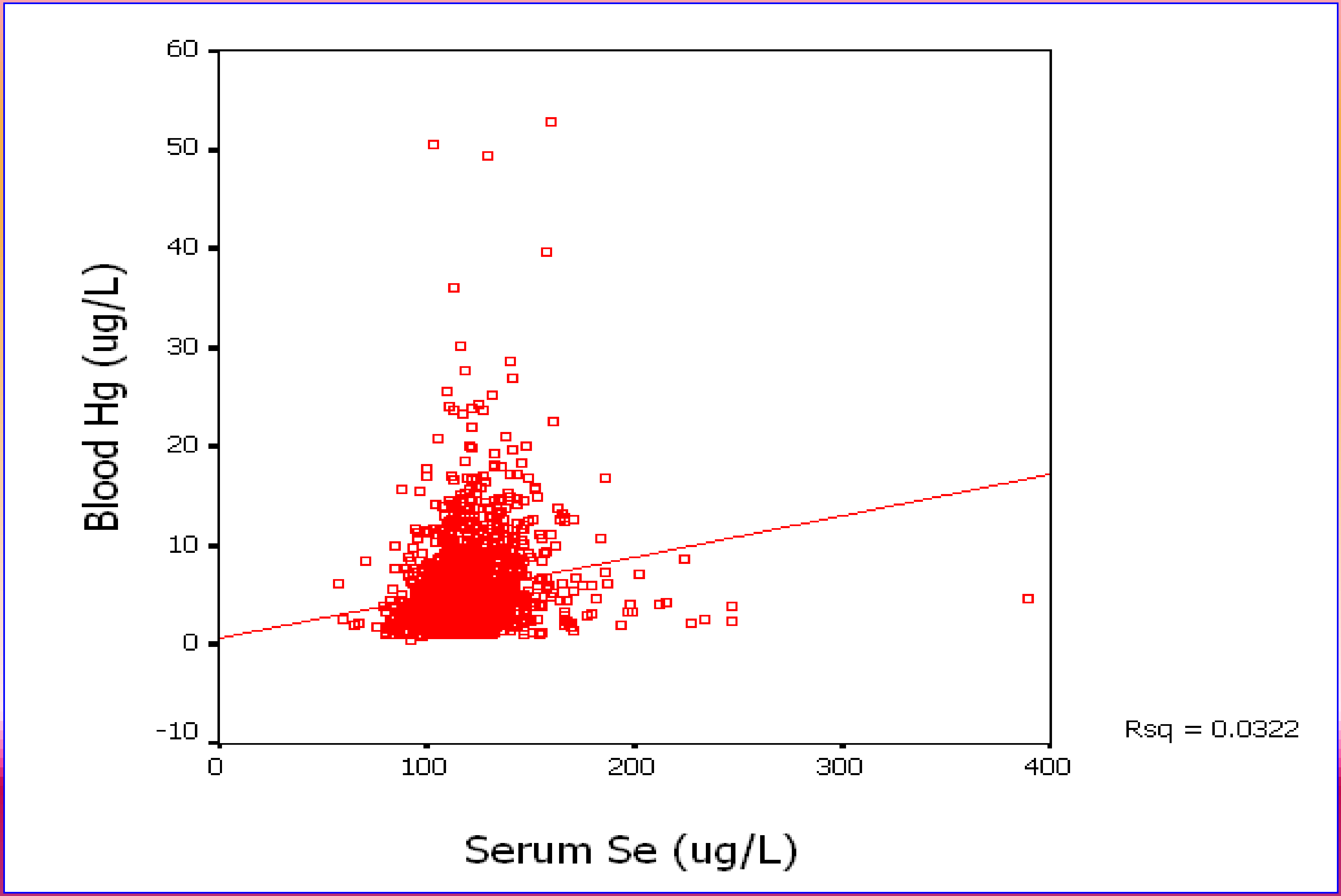


Fig 8. Association between blood Hg and serum Se levels

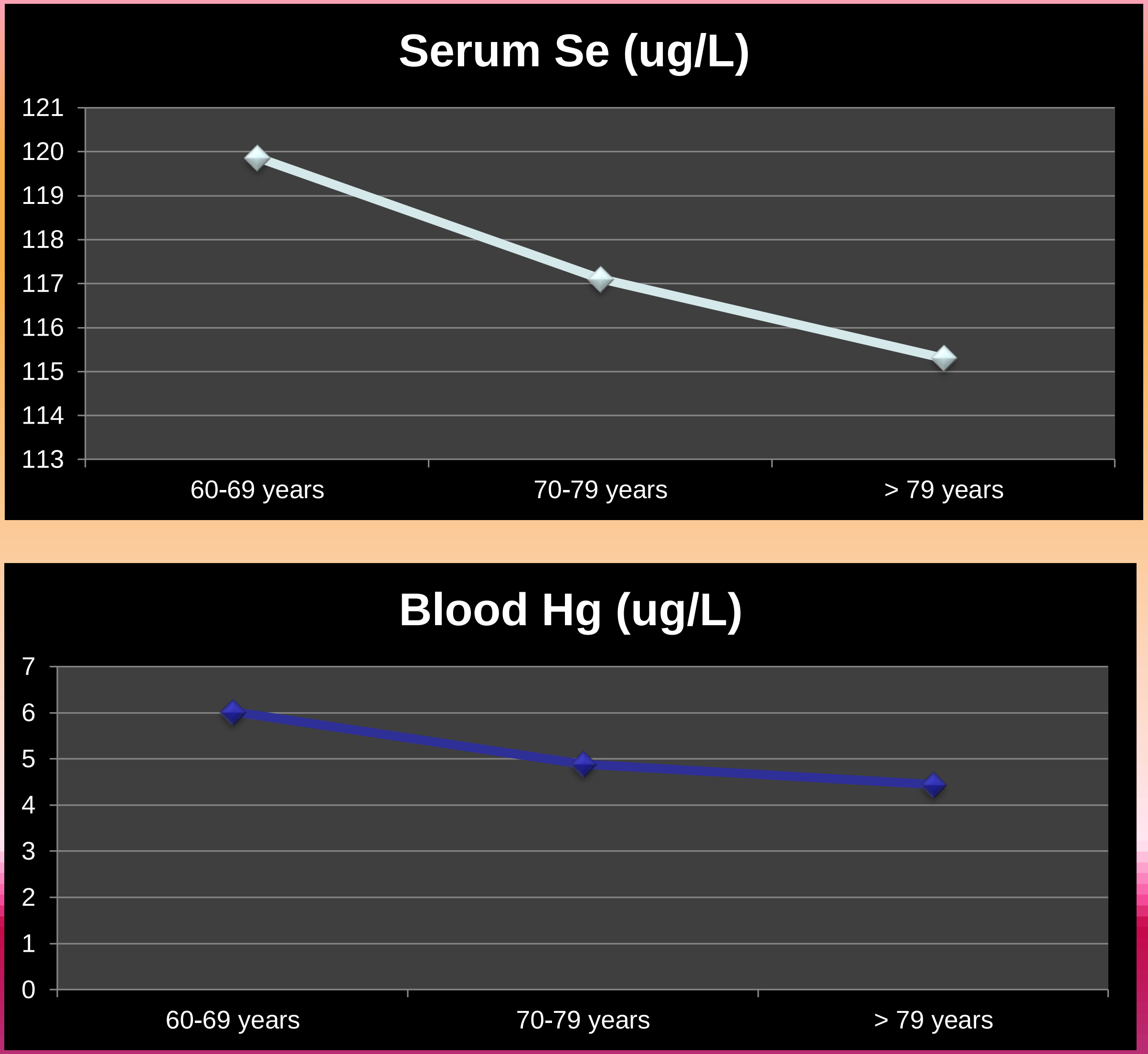


Fig 9. Blood Hg and serum Se levels , classified by 3 age groups

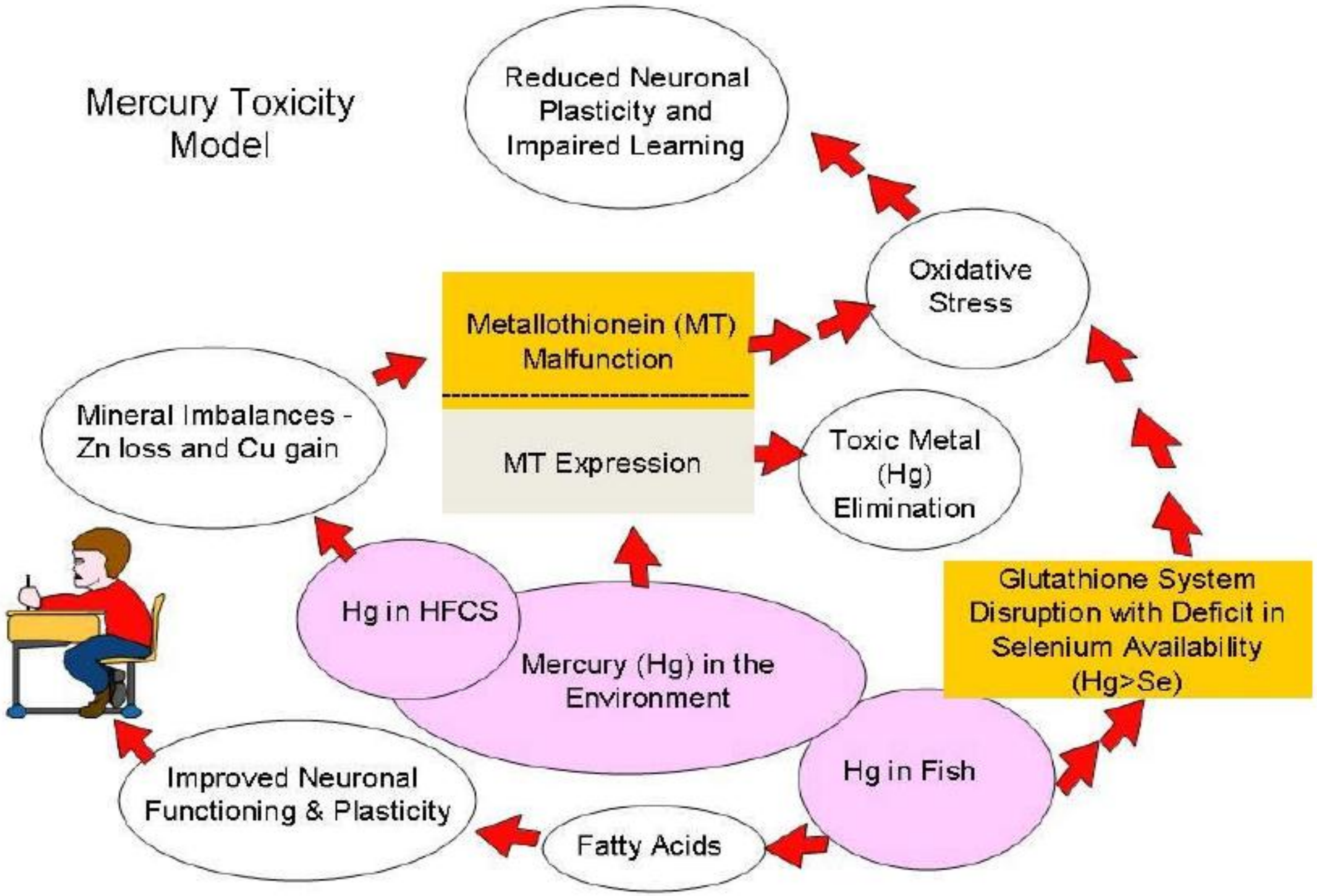


Figure 1
Mercury Toxicity Model.

Food rich in selenium

Food	Micrograms of Selenium
Cod, cooked, dry heat, 3 oz	40
Tuna, canned, 3 oz	69
Shrimp, 4 oz	45
Turkey, breast, oven roasted, 3 1/2 oz	31
Spaghetti w/ meat sauce, 1 cup	25
Chicken, meat only, 1/2 breast	24
Bread, enriched, whole wheat, 2 slices	20
Oatmeal, 1 cup cooked	16
Cottage cheese, low fat 2%, 1/2 cup	11
Rice, enriched, long grain, cooked, 1 cup	14

Mahidol University
Wisdom of the Land

New published Paper

- Results from EGAT 2/1 and 2/3

Hindawi Publishing Corporation

Jintana Sirivarasai Update My Account Logout

BioMed Research International

Impact Factor 2.436

Author Activities

BioMed Research International (formerly titled Journal of Biomedicine and Biotechnology)

Association Between Inflammatory Marker, Environmental Lead Exposure, and Glutathione S-Transferase gene

Jintana Sirivarasai[1]*, Winai Wananukul[1], Sming Kaojarern[1], Suwannee Chanprasertyothin[2], Nisakron Thongmung[2], Wipa Ratanachaiwong[3], Thunyachai Sura[1], and Piyamit Sritara[1]

[1]Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, 10400 Thailand
[2]Office of Research Academic and Innovation, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, 10400 Thailand
[3] Health Office, Electricity Generating Authority of Thailand, Nonthaburi, 11130, Thailand

***Correspondence: Jintana Sirivarasai, Ph.D**
Division of Clinical Pharmacology and Toxicology, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand
Tel: +66 (0) 2201 1620 Fax: +66 (0) 2201 1631
E-mail address : jintana.sir@mahidol.ac.th

Table 1 :Means of blood lead levels and other variables classified by 4 lead-quartiles among men participating in the EGAT STUDY PROJECT

Characteristic	Blood lead Quartile				
	Total (N=924)	Quartile 1 (N=218)	Quartile 2 (N=222)	Quartile 3 (N=242)	Quartile 4 (N=242)
Blood lead level, mean (rang), µg/dL	5.45 (1.23-24.63)	2.44 (1.23-3.47)	3.95 (3.48-4.55)	5.77 (4.56-6.47)	9.21 (6.48-24.63)
Age, mean (SD), years	42.55 (3.15)	42.94 (6.33)	42.17 (5.29)	42.33 (5.29)	42.78 (7.30)
Body mass index, mean (SD), kg/m^2	23.99 (6.11)	24.59 (3.25)	23.56 (6.21)	23.78 (9.19)	24.06 (6.24)
Mean blood lead (SD), µg/dL; classified by smoking status					
No-smokers	4.93 (2.36)	2.09 (0.96)	3.79 (0.88)	4.90 (1.01)	8.76 (1.12)
Former smokers	6.07 (2.94)	2.45 (0.75)	3.68 (1.23)	4.81 (0.97)	9.23 (1.39)
Current smokers	9.29[a] (4.26)	2.81 (1.21)	4.08 (1.08)	5.43 (1.14)	12.34 [a,b] (5.32)
Mean blood lead (SD), µg/dL; classified by alcohol consumption,					
Non-drinkers	5.32 (2.36)	2.12 (0.96)	3.56 (1.12)	4.84 1.24)	7.96 (3.12)
Light-drinkers	4.96 (1.98)	1.99 (0.35)	3.78 (1.04)	5.12 (1.98)	8.82 (3.07)
Ex-drinkers	5.17 (2.18)	2.32 (0.74)	3.44 (1.31)	4.97 (1.69)	8.23 (2.98)
Current drinkers	6.49 (4.99)	2.41 (1.01)	4.17 (1.36)	5.33 (1.54)	11.07 (5.31)
Serum hs-CRP level, mean (SD), mg/L	2.07 (1.62)	1.54 (0.79)	1.87 (0.96)	2.79 (1.36)	4.12 [c,d] (2.18)
Systolic BP, mean (SD), mmHg	124.4 (10.55)	114.8 (6.09)	123.7 (8.06)	126.8 (10.14)	132.1[c] (16.13)
Diastolic BP, mean (SD), mmHg	77.29 (15.38)	77.44 (8.73)	76.78 (11.75)	77.62 (16.83)	77.31 (10.77)

[a,b] Significantly different from never smoked and former smoker, respectively, $p < 0.01$
[c'd] Significantly different from blood lead quartile 1 and 2, respectively $p < 0.01$

Table 2: Genotype frequencies for GSTP1, GSTM1 and GSTT1 (N=924)

Gene	Variation	Genotype	Frequency	
			Number	Percentage
GSTP1 (rs1695)	Ile105Val	Ile/Ile	517	55.9
		Ile/Val and Val/Val	407	44.1
GSTM1	Deletion	+/+	484	52.4
		-/-	440	47.6
GSTT1	Deletion	+/+	286	30.9
		-/-	638	69.1
GSTM1 and GSTT1	Deletion	+/+	161	17.4
		-/+ or +/-	448	48.5
		-/-	315	34.1

Table 3: The odds ratio (OR) for increasing inflammatory mark by genetic variations of GSTs in relation to blood lead level > 6.47 μg/dL

GST genetic variation	CRP*	
	OR	95% CI
GSTP1 (Ile105Val)		
Ile/Ile	1	Reference
Ile/Val and Val/Val	1.46	1.05-2.20
GSTM1		
+/+	1	Reference
-/-	1.32	1.03-1.69
GSTT1		
+/+	1	Reference
-/-	1.65	1.17-2.35
GSTM1 and GSTT1		
+/+	1	Reference
+/ or -/+	1.07	0.88-1.31
-/-	1.98	1.47-2.55

CRP : C-reactive protein; OR : odds ratio; CI : Confidence interval

*With adjustment for age, body mass index, smoking status, alcohol use and blood pressure

Mahidol University
Wisdom of the Land

Acknowledgement

- การไฟฟ้าฝ่ายผลิตแห่งประเทศไทย
- คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล
- แหล่งทุนสนับสนุนโครงการวิจัยฯ.
- ศาสตราจารย์ปิยะมิตร ศรีธรา
- อาจารย์ นายแพทย์ปริญญ์ วาทีสาธกกิจ
- เจ้าหน้าที่ทีมทำงานทั้งหมดในการเก็บข้อมูลและเก็บตัวอย่างเลือด

Jintana Sirivarasai, Ph.D

Division of Clinical Pharmacology and Toxicology
Department of Medicine
Faculty of Medicine Ramathibodi Hospital