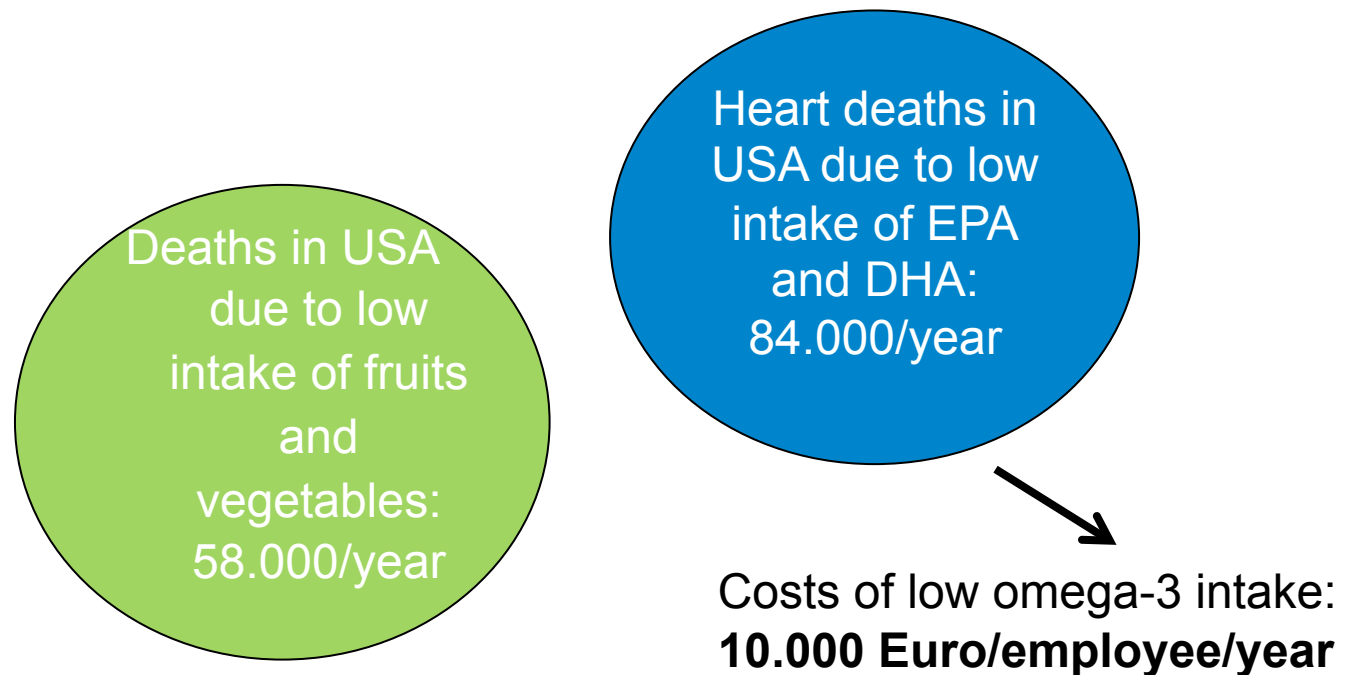


Environmental pollutants in fish oil products and the importance of efficient removal



Introduction - Motivation



Is it healthy to eat more fish?

The New York Times

December 12, 2012

If Mercury Pollution Knows No Borders, Neither Can Its Solution

By KATE GALBRAITH

AUSTIN, TEXAS — The harm that can be caused by consuming or breathing mercury is well known and terrible. A pregnant woman, eating too much of the wrong kind of fish, risks bearing a child with neurological damage. Adults or children exposed to mercury can experience mood swings or tremors, or sometimes even respiratory failure or death.

BBC NEWS

Fish pollutants' link to diabetes

More evidence has emerged suggesting a link between pollutants found in oily fish and type two diabetes.

An international team found high levels of persistent organic pesticides (POPs) in the blood correlated to insulin resistance, a precursor to diabetes.

POPs are stored in fatty tissues - the study suggested this may be why obese people are more vulnerable to diabetes.

MailOnline

Fish from polluted rivers 'can trigger breast cancer'

POPs – Persistent organic pollutants

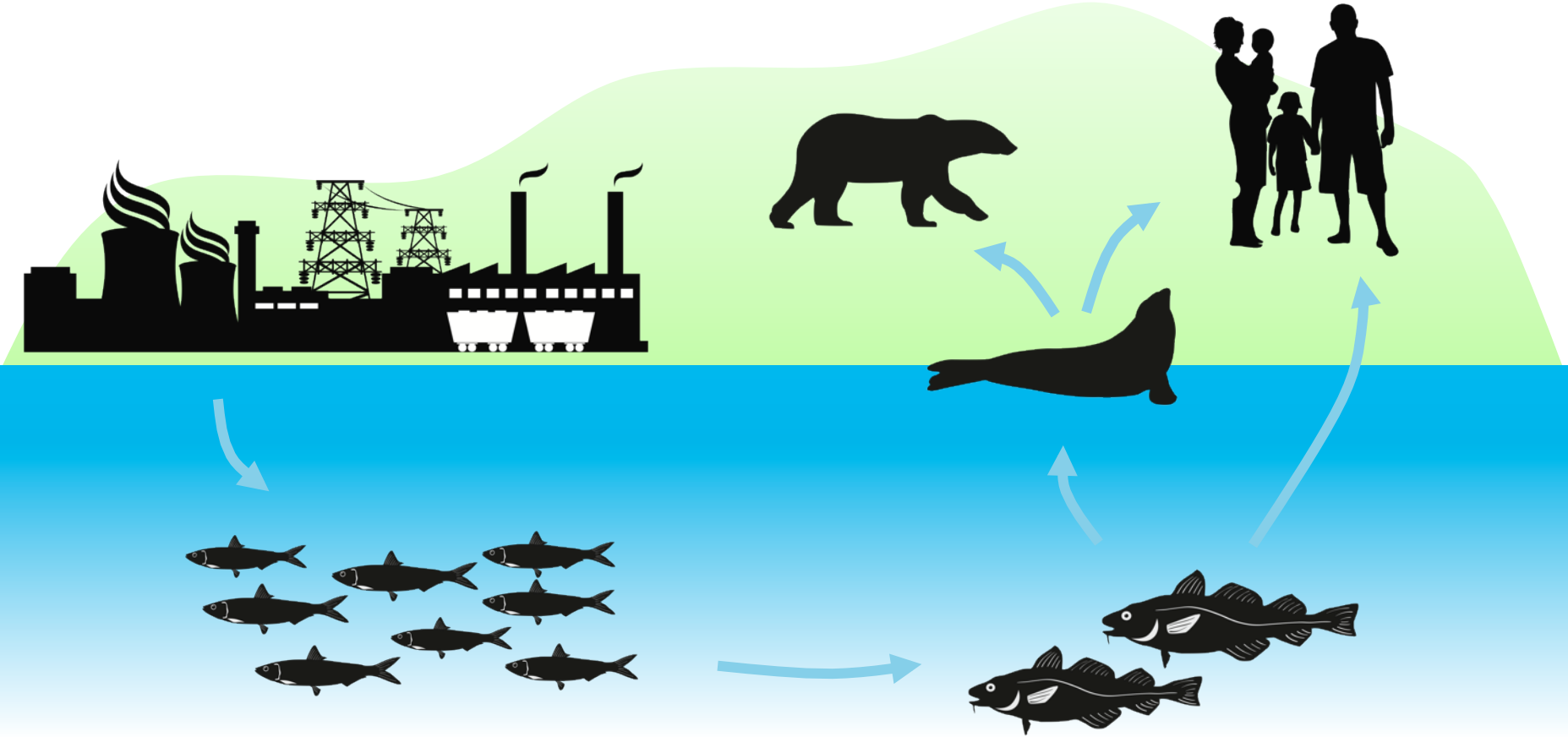
Man-made chemical substances like

- PCB
- dioxins
- DDT
- Brominated Flame Retardants (BRF)
- Persistent
- Long-range transport
- Lipophilic
- Toxic

Dioxin- a persistent environmental pollutant



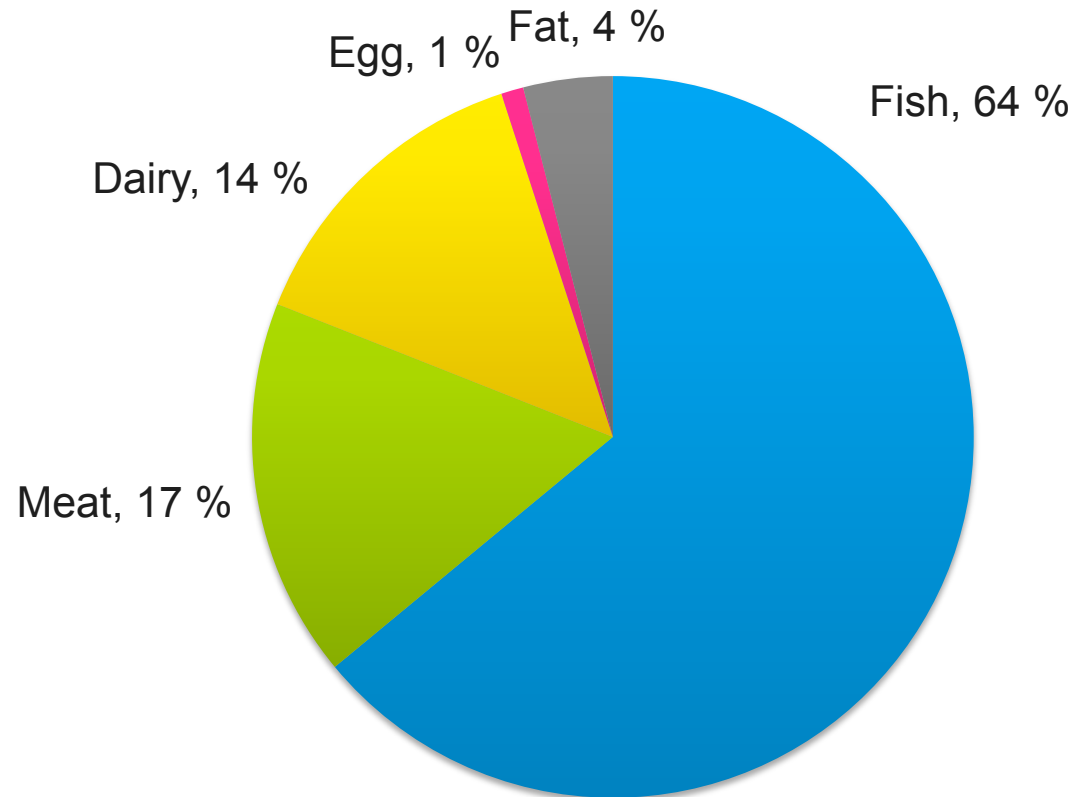
POPs accumulate in the food chain



Fish is the main source of PCB

PCB intake from the market basket

Relative contributions



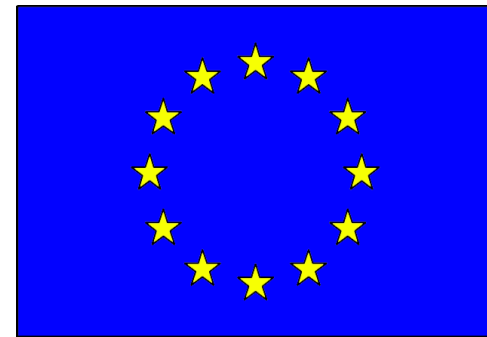
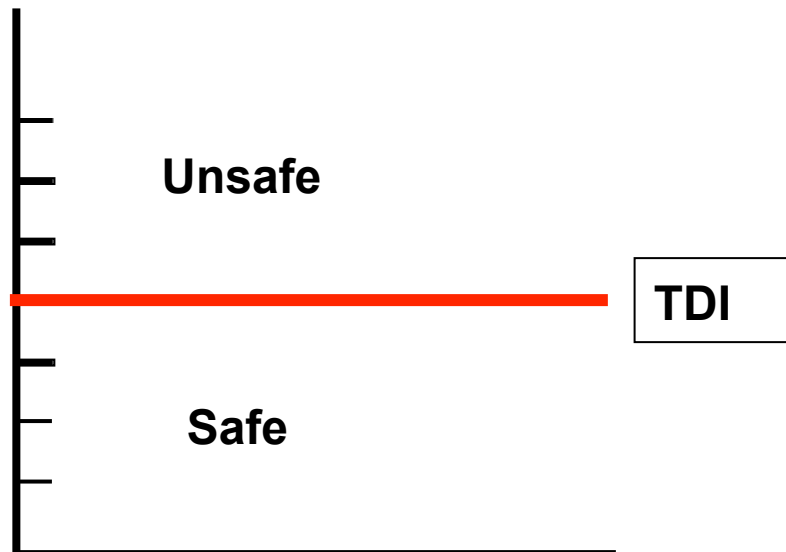
POPs are passed on to the next generation

- POPs cross placenta
- High concentrations in breast milk
- Babies receive daily doses exceeding safe limit
- Still, breast feeding is strongly recommended



Alcock *et al.* 1999; Kimbrough *et al.* 2010

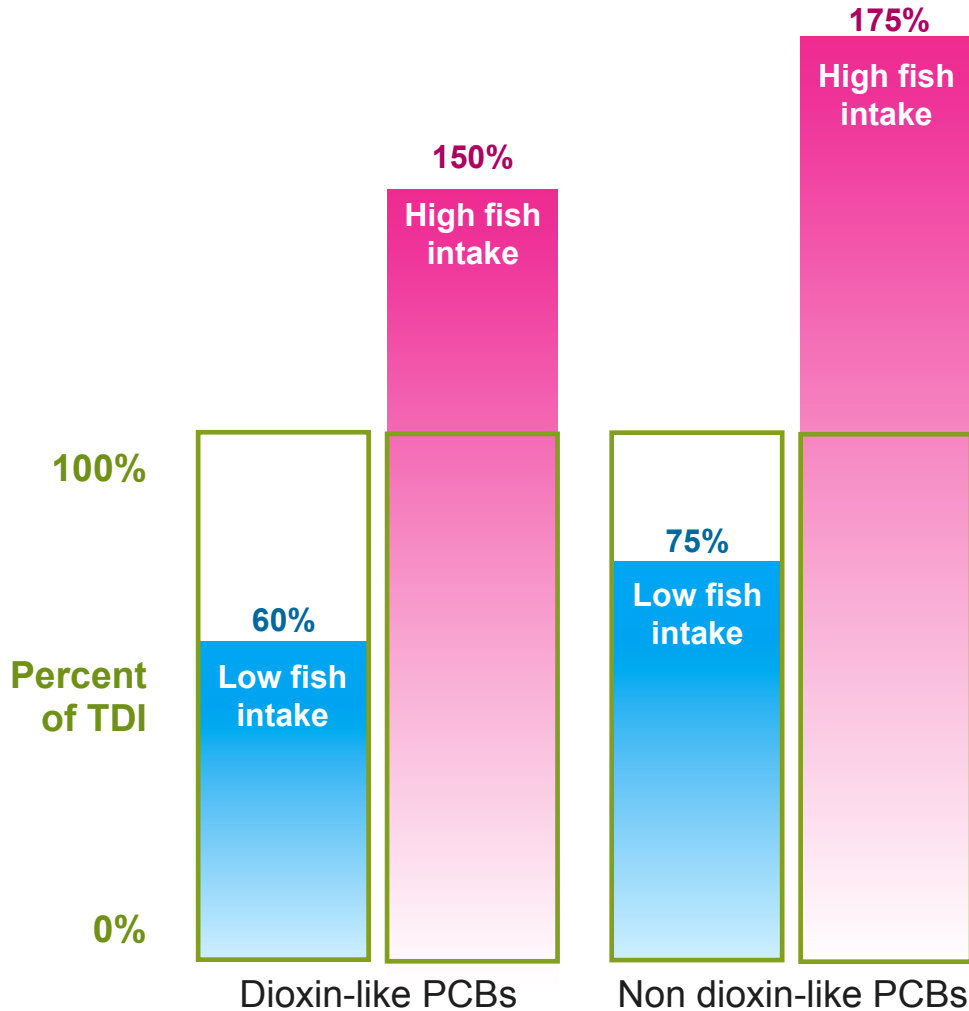
Limits are set by health authorities



Tolerated Daily Intake: The amount that can be ingested daily over a lifetime without considerable health risk



INTAKE THROUGH FOOD CAN EXCEED TOLERATED DAILY INTAKE (TDI)



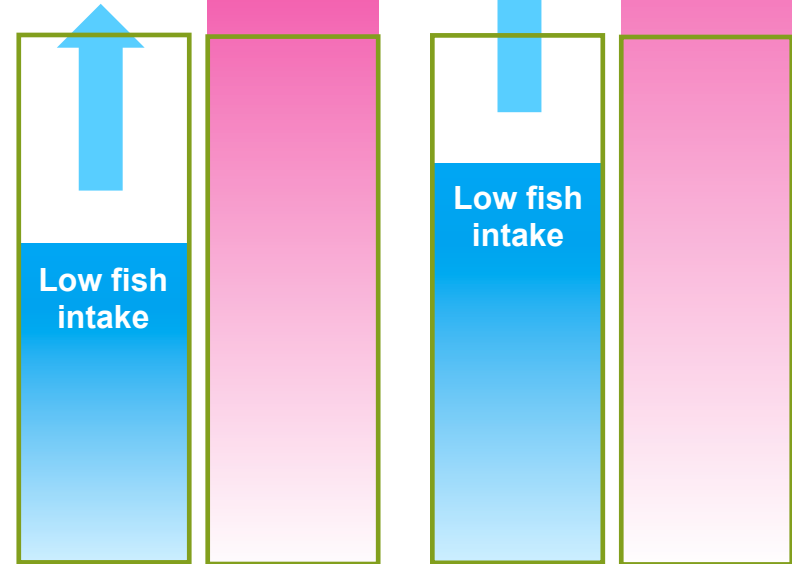
	Dioxin-like PCBs (pg/kg/day)	Non-dioxin-like PCBs (ng/kg/day)
TDI	1-4	20*
Estimated daily intake	1.2-3.0	15-35

Rocca and Mantovani 2006

VARIOUS OMEGA-3 SUPPLEMENTS GIVE EXPOSURE ABOVE TDI ALONE

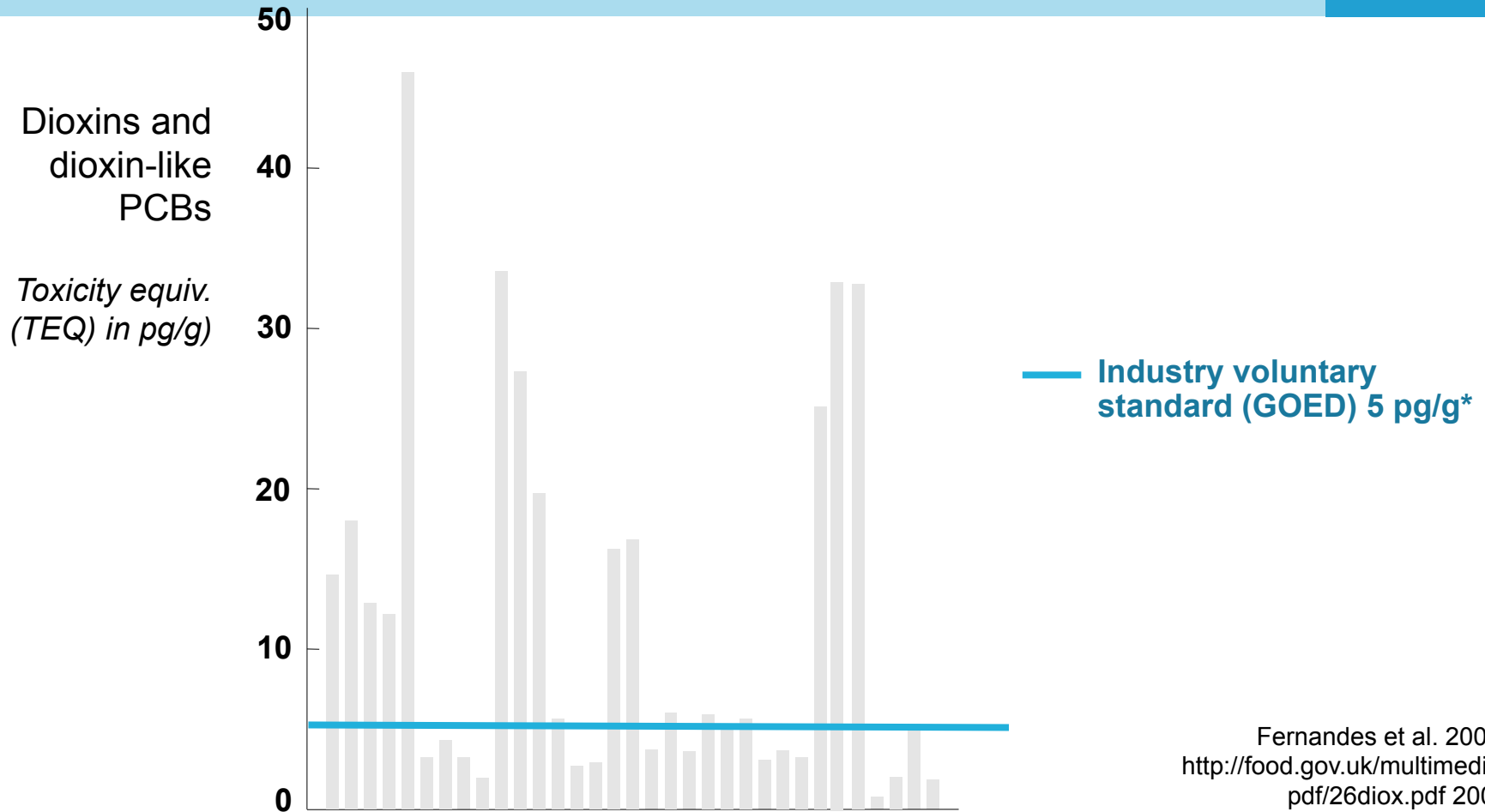


100%
Percent
of TDI
0%



Fernandez *et al.* 2006

High levels of pollutants are common in fish oil supplements



Fernandes et al. 2006;
<http://food.gov.uk/multimedia/pdf/26diox.pdf> 2002

Biological effects



Many adverse health effects associated with POPs

- **Metabolic effects**
 - Diabetes and metabolic syndrome

- **Neurodevelopmental problems**
 - Learning and behavior problems in infants

Many adverse health effects associated with POPs

- **Metabolic effects**

- Diabetes and metabolic syndrome

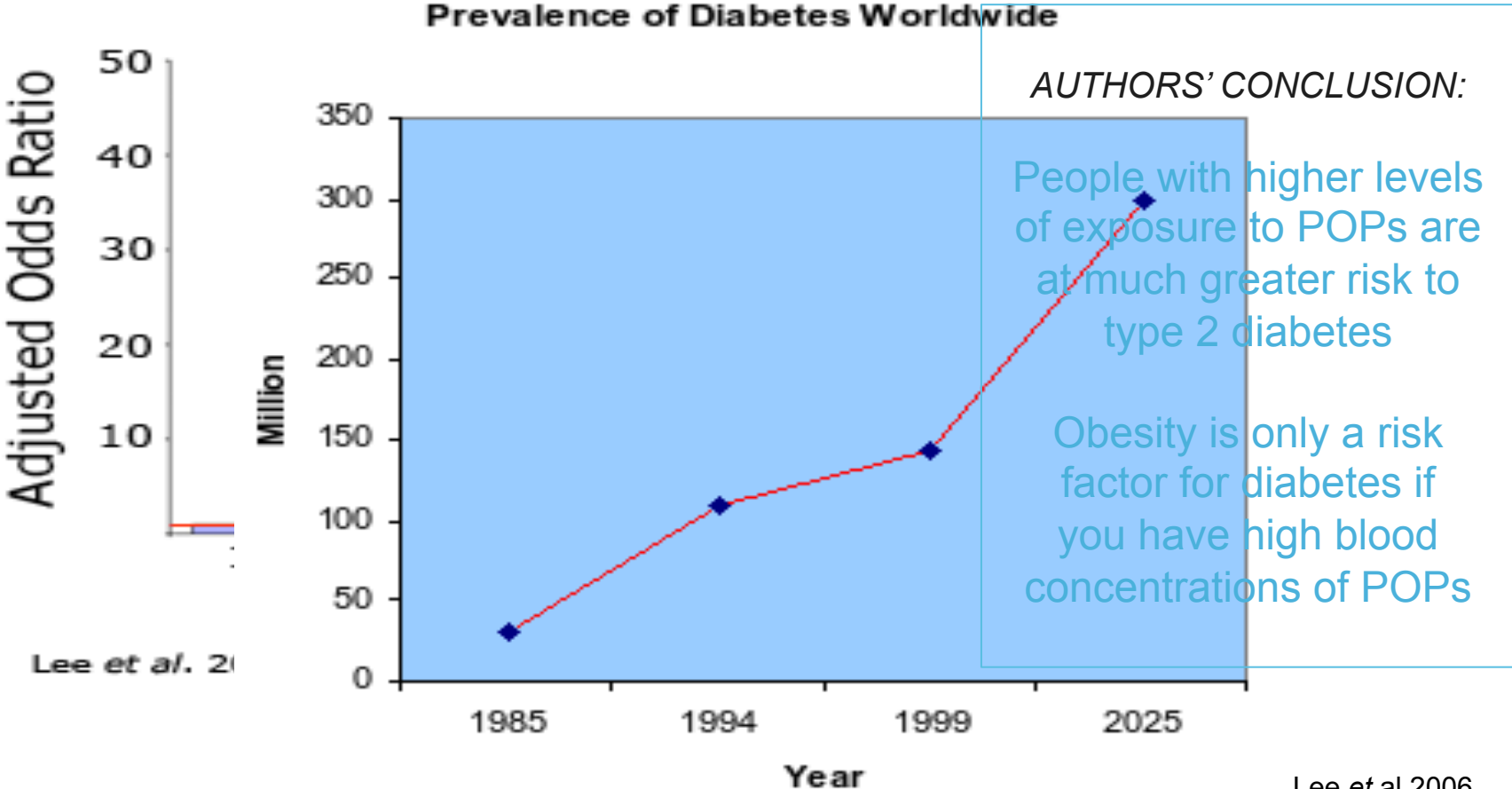
- **Neurodevelopmental problems**

- Learning and behavior problems in infants

- **Cancer**

- PCB is classified as probable carcinogen
- Excess mortality reported from various cancers forms in highly exposed areas

Increased diabetes prevalence linked to POPs exposure



Adjusted Odds Ratio

Lee et al. 2006

POPs promote insulin resistance and metabolic disorders

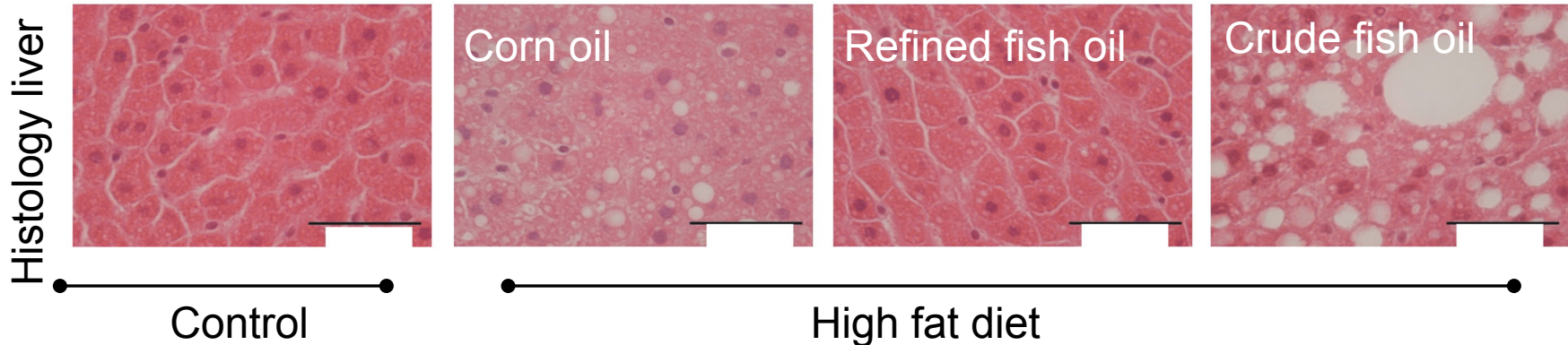
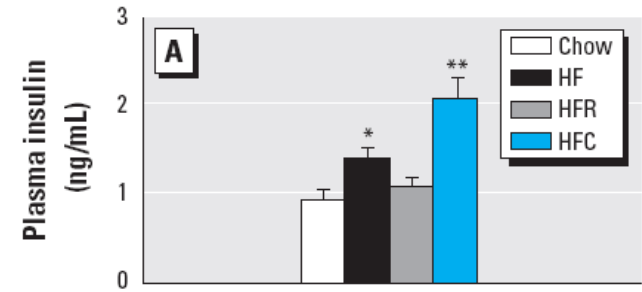
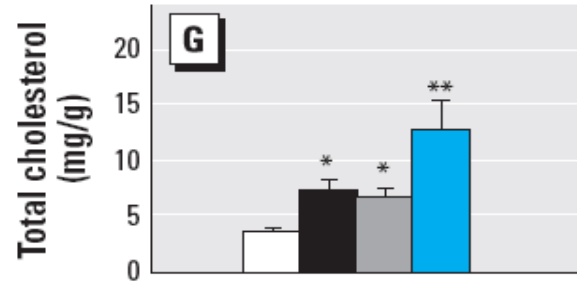
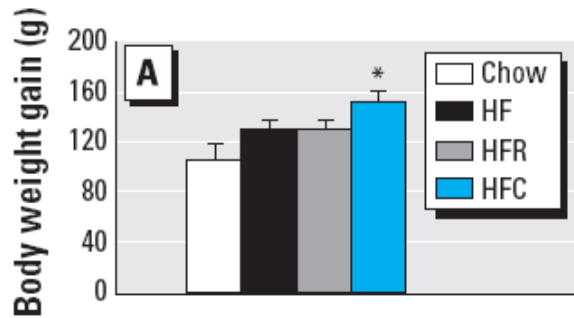
Exposure to POPs increases the risk of developing insulin resistance and metabolic disorders

Ruzzin et al. 2010

Experimental Model:

- Rats fed salmon oil with and without POPs for 4 weeks
 - Oil was made from fish aimed for human consumption
 - Assessment of body weight, insulin sensitivity, lipid parameters and hepatosteatosis
- Treatment groups:
 - Control feed
 - High fat diet with 20% corn oil
 - High fat diet with 20% refined fish oil (low POPs)
 - High fat diet with 20% crude fish oil (high POPs)

Exposure to POPs (cont.)



Rats exposed to crude, but not refined, salmon oil developed insulin resistance, abdominal obesity, and hepatosteatosis

Metabolic syndrome and diabetes type 2

- Metabolic syndrome is a risk factor for diabetes 2 and precedes the onset with one or two decades
- The prevalence worldwide is increasing dramatically
- Established risk factors are sedentary life style, smoking, age and high BMI



METABOLIC SYNDROME

Central obesity
High blood pressure
High TG
Insulin resistance

High levels of POPs a strong risk factor for metabolic syndrome

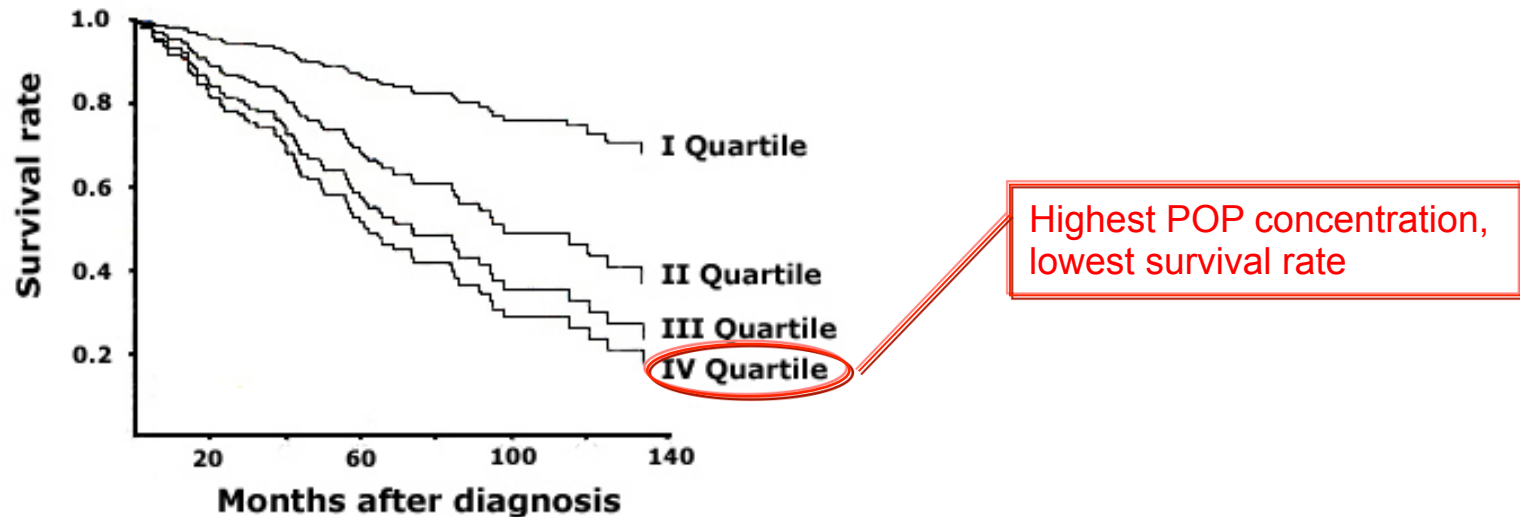
Odds ratio for specific metabolic syndrome criteria by quartile of PCBs in serum

Criteria	PCB 1 st quartile	PCB 2 nd quartile	PCB 3 rd quartile	PCB 4 th quartile	p value
BMI \geq 25kg/m ²	1.0	1.7	1.8	2.6	<0.01
Blood pressure \geq 130/85 mmHg	1.0	1.0	1.1	1.9	<0.01
Triglycerides \geq 150 mg/dl	1.0	2.4	3.4	5.2	<0.01
HDL \leq 40mg/dl females HDL \leq 50mg/dl males	1.0	1.1	1.9	2.1	<0.06
HbA1c (\geq 5.6%) or physician diagnosis of T2DM)	1.0	2.1	3.1	8.0	<0.01

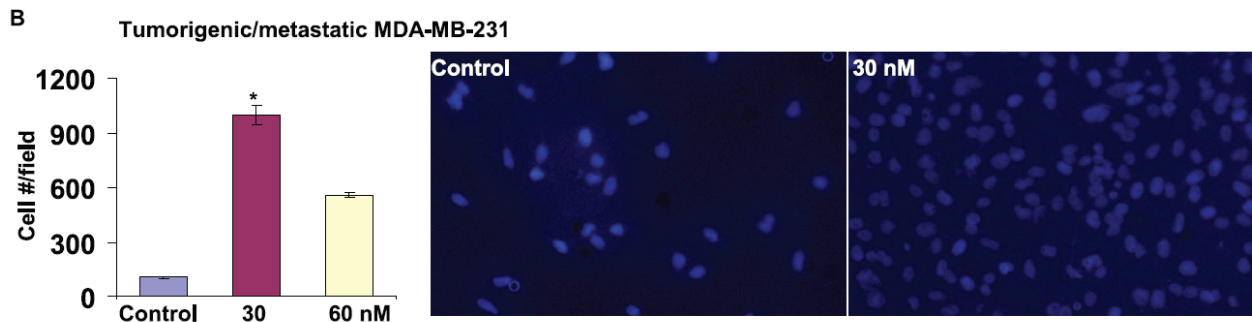
Adapted from Uemura et al. 2009

Persistent Organic Pollutants (POPs) and malignancies

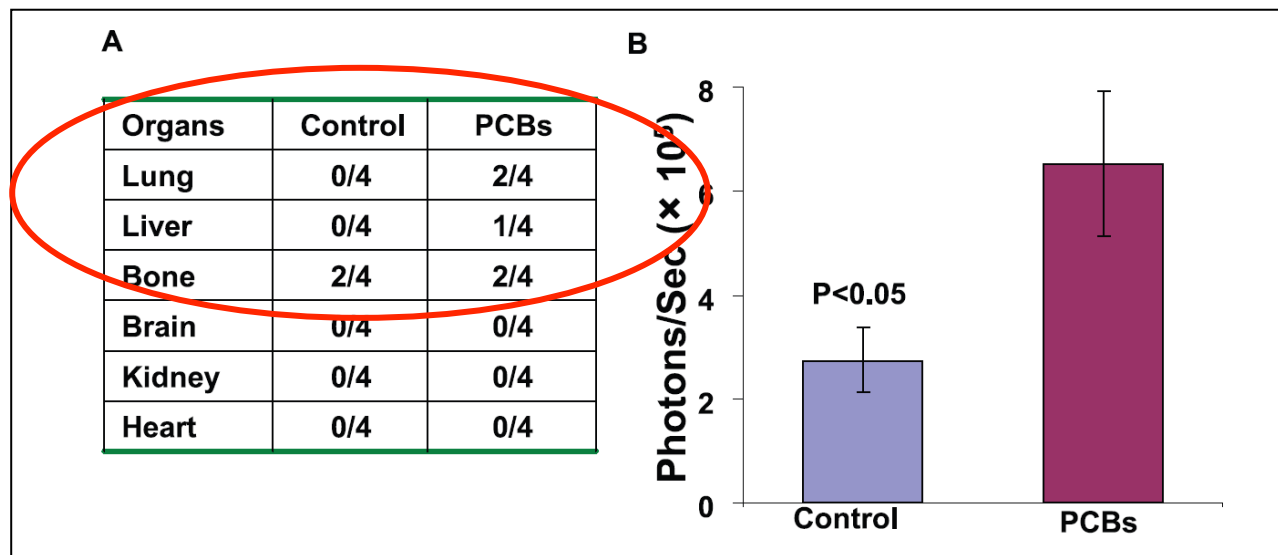
- In brain, liver, breast, skin and more
- Pollutant burden is correlated with more aggressive and metastatic breast cancers with a poorer survival rate



PCBs Enhance Metastatic Properties of Breast Cancer Cells



Increased motility in PCB exposed tumour cells.



Increase number of tumours in PCB exposed mice.

POPs and development of brain functions

- The brain receives a large portion of the accumulated PCBs.
- Many studies made on cognition and motor development in early childhood and school age.
 - Majority of all studies made show a clear negative effect of PCB exposure on cognition in children (reviewed in Schantz *et al* 2003)
- Association between low-level POPs exposure and ADHD-like behavior (Sagiv *et al.* 2010)



POPS and development of brain functions

Drawings by children in the foothills



4-year-olds

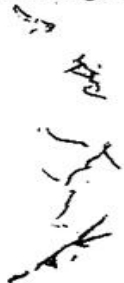


5-year-olds



Area of No Pesticide Use

Drawings by children in the valley



4-year-olds



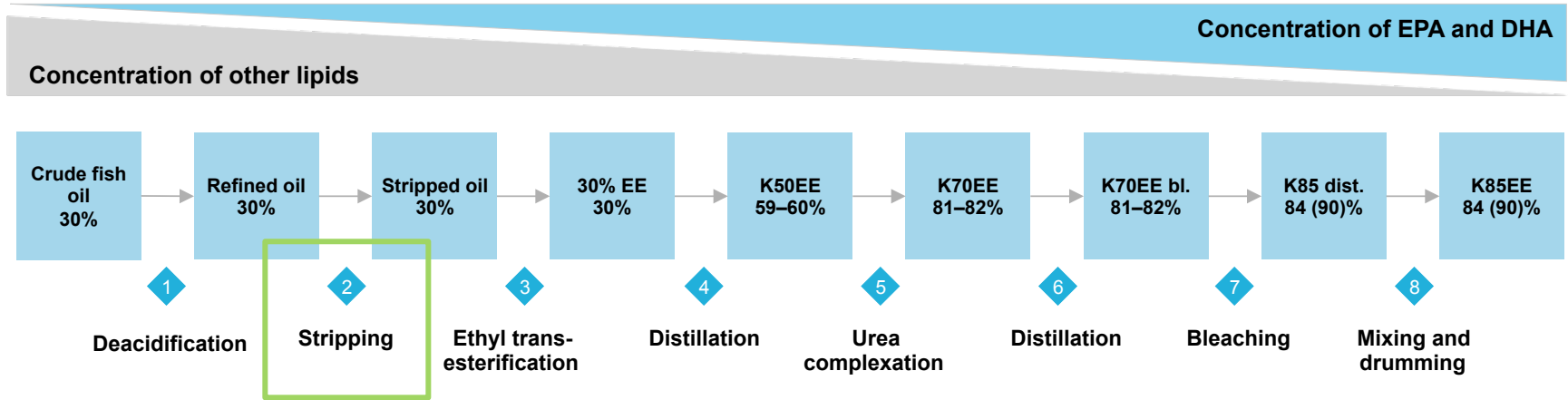
5-year-olds

Area of Pesticide Use

Removing pollutants



Pollutants can be removed during manufacturing



- Pollutants are stripped early in the production process
- Early removal prevents up-concentration of pollutants at later stages

- Short-path distillation with working fluid removes pollutants but not EPA/DHA

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Removal of persistent organic pollutants in fish oils using short-path distillation with a working fluid

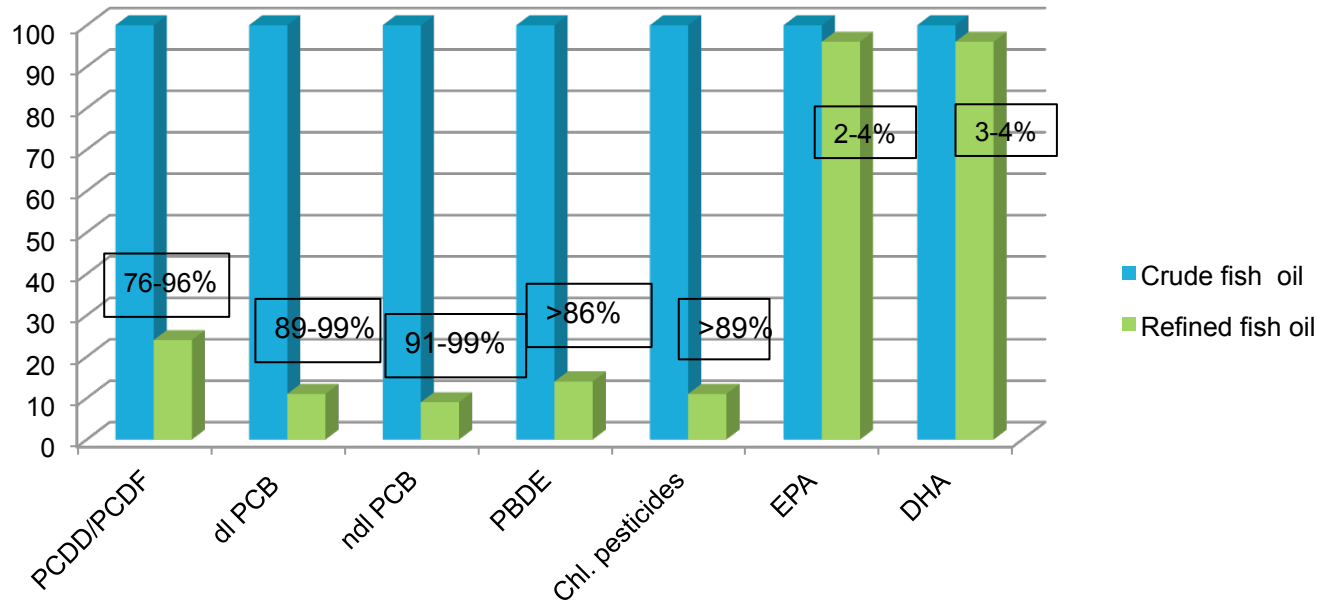


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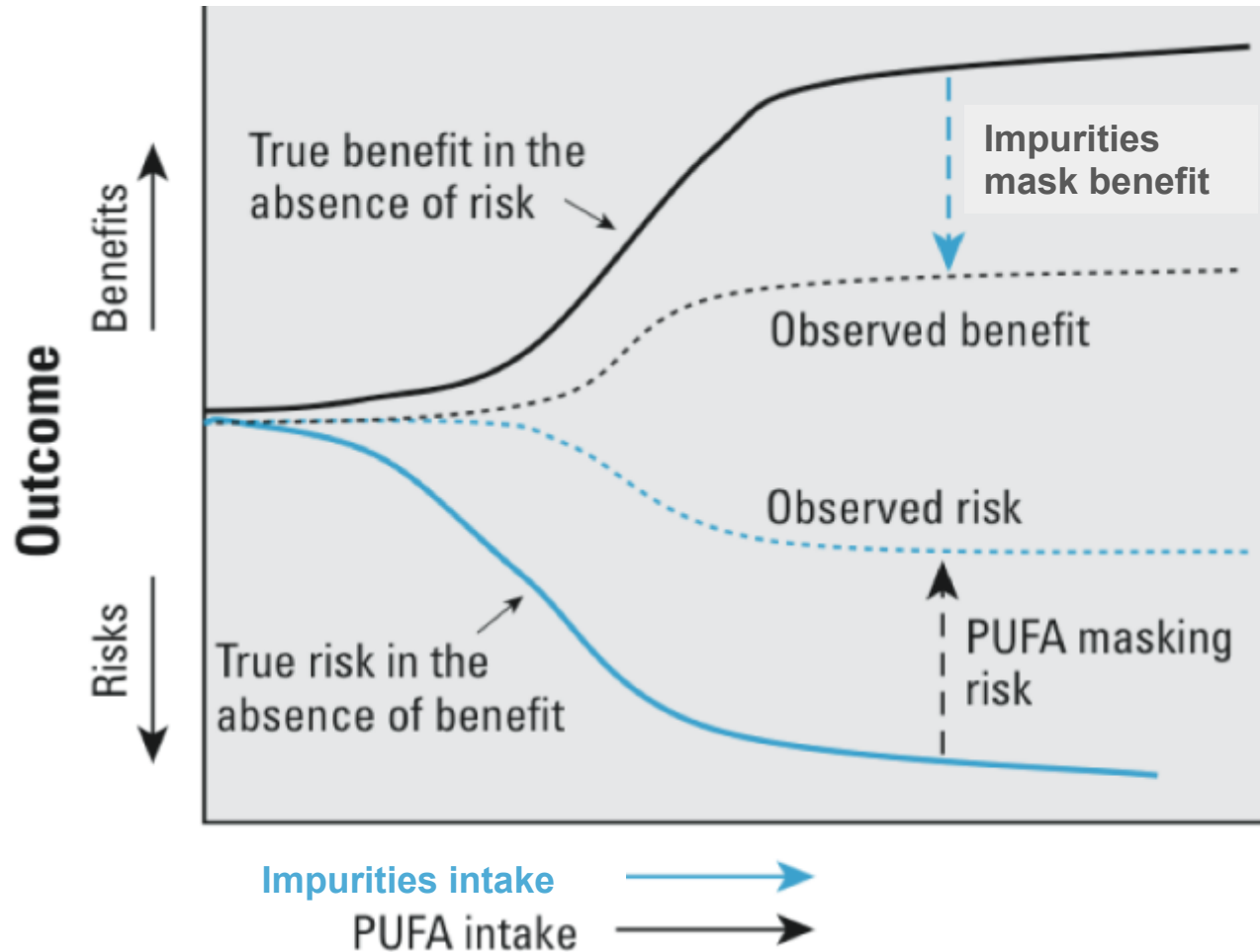
^b Neperdo Biomarine, Asphaugen, NO-8140 Innøyr, Norway

^c Pronova BioPharma Norge AS, P.O. Box 2109, NO-3202 Sandefjord, Norway



Taking home message

Balance of risk and omega-3 benefits



Take home messages

- **POPs are toxic to humans**
- POPs are lipophilic and accumulate in crude fish oil, but may be efficiently removed.
- To promote health the **purity of the Omega-3 product is critical**



THANK YOU FOR YOUR ATTE





02

Q & A

Measurement of environmental contaminants in globally-represent samples of fish oil supplements

GOED Nutrasource (sampling 2005-2010)

- Abstract: 1894 fish oil samples were analyzed against GOED Voluntary Monograph.
- 44 brands from 8 countries over 6 years.
- Mean EPA/DHA concentration in all 1894 samples 38.39%
- PCB analyses:
 - DL PCBs 297
 - NDL PCBs: 683
- Concentration of PCB reported as:
 - EPA/DHA \leq 50% (167 samples –whereas 57% samples in 2010)
 - EPA/DHA \geq 50% (516 samples –whereas 42% in 2010)

Number of brands?

Number of brands?

- EPA + DHA number samples:1894 mean 38.39 StE 0.6261
- $\sqrt{1894}= 43,5$
- Standard dev $0.6261 \times 43.5=27,24$
- 95th percentile: $2 \times 27,24= +/- : 54,5$

Published PCB and TEQ levels in consumer products around the world.

Sum of PCBs and TEQs measured in fish oils around the world. Dioxin-like PCBs constitute 60-90% of the TEQ value

Component	Country	TEQ pg/g	Sum PCBs ng/g	Reference
Salmon oil	Canada	70.1	36-105	Bourdon et al., 2010
Salmon oil	Canada	18.0	36- 170	Rawn et al., 2009
Cod liver oil	UK	12.9-46.0	153	Fernandes et al., 2006
Cod liver oil	Spain	9.4-14.5	49.7-98.3	Marti et al., 2010
Cod liver oil	Ireland	0.6-37.6		Marti et al., 2010
Fish oil	Japan	1.3-29.5		Marti et al., 2010

TK model of EFSA 2005 giving TDI for NDL PCB

- BMDL (neurological/immune effect after perinatal exposure) $1\mu\text{g}$ PCB/kg lipid in mothers, effect after total exposure of all PCBs)
- Daily intake of $40\text{ ng PCBs/kg body weight/day}$ result in serum level of $1\mu\text{g PCB/g lipid}$.
- 6 indicator NDL PCB constitute 50 % of the BMDL value of $1\mu\text{g PCB/g lipid}$ (assumption) = $0.5\mu\text{g PCB}_6/\text{g lipid}$

=20 ng PCB₆/kg body weight /day

- EFSA have monitored the levels of PCB and dioxin in all food items for many years.
- EFSA in 2012, The conclusion in the report where that the average exposure vary 0.57 -2.54 (30-130% of TDI), and the 95th percentile were between 1,2-9,9 pg TEQ/kg which is 60-495% of TDI.
- Also, that 1-52,9 % of the population are estimated to exceed the limit of 14pg/kg/week

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