



Exponent[®]

**TRUTH AND CONSEQUENCES IN RISK
ASSESSMENT AND MANAGEMENT**

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Risk Management Objective

Do No Harm

Risk Management Objective

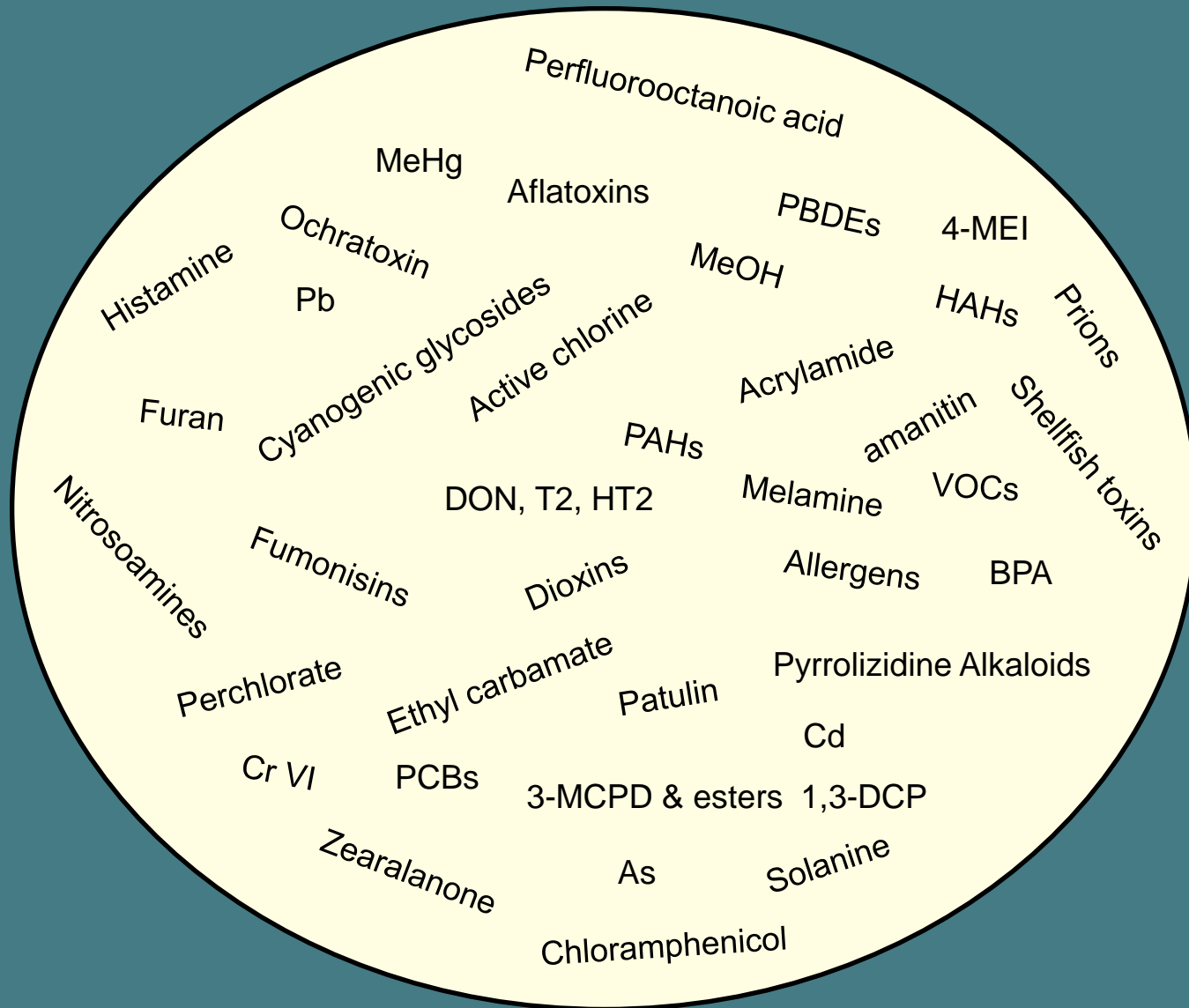
Reasonable Certainty that Risk Management Results in Net Positive Public Health Impact

One Chemical Focus

Conservative Risk Assessment

- **Safety assessment approach for threshold cases**
 - Factors of 10 approach may be overly conservative
- **‘Linear’ extrapolations for non-threshold carcinogens or threshold carcinogens w/o definitive mechanistic data**
 - Orders of magnitude extrapolation may result in a risk estimate that is much much greater than the actual risk
- **When exceed safety or risk standard, such as Provisional Tolerable Daily Intake (PTDI), minimize to the extent feasible**

Real World of Chemicals in Foods



Real World of Multiple Hazards



Risk Equation

$$\Delta\text{Risk} = \Delta R_{\text{Chem1}} + \sum \Delta R_{\text{Chem2-x}} \\ + \sum \Delta R_{\text{Micro1-y}} + \sum \Delta R_{\text{Nutri1-z}} \\ + \sum \Delta R_{\text{Misc}}$$

- Chemical risks assessed conservatively
- Nutritional benefits assessed conservatively
- Leads to bias in ΔRisk

CCFAC - Aflatoxins

- Late 90s aflatoxins in peanuts was major issue
- European Union (EU) wanted a Maximum level (ML) = 10 ppb and even 5 ppb in peanuts for further processing compared to 20 ppb in U.S.
- Debate eventually boiled down to 15 ppb vs 10 ppb
- US wrote a long comment arguing that based on distributions of aflatoxins in peanuts over the years, the difference in average exposure between an ML of 10 & 15 ppb was 0.1 ppb
- Calculated this to be about 1 in 10 million risk
- Nordic countries stated it should be 1 in a billion
- 15 ppb eventually prevailed in 1999

CCFAC - Aflatoxins

- Why is 10 ppb a problem – the consequences?
- Difficult to meet in developing countries
- Developing countries have high incidence of Hept B – aflatoxin B₁ potency is 30 x higher for Hept B + individuals
- Unnecessarily low levels will result in retention of more contaminated product by developing country
 - Results in reduced available food
 - Consumption of more contaminated food where the risk is highest due to Hept B (Kenya – aflatoxicosis 2004 thru 2006)
 - Subsistence farmers have lower income and fewer break out of subsistence trap

CCFAC – Active Chlorine

- **1998 – Fish Committee: Concern about use of chlorine to reduce microbial loads**
- **2000 – Fish Com: Disc paper – scientific evidence does not warrant changing 10 ppm chlorine recom.**
- **2001: Denmark raises concern again in Codex Committee on Food Additives and Contaminants (CCFAC)**
- **Significant concern in US: potential for increased microbial and pathogen loads especially from products like shrimp from developing countries**
- **2002 – 2004: Discussion papers and draft Code of Practice (Denmark lead) – included advocating not permitting use until risk assessment done**

CCFAC – Active Chlorine

- **US strategy: a risk – benefit assessment needed to be done.**
- **2008 FAO/WHO expert consultation:**
 - ‘No health concerns were identified from an evaluation of the toxicity and dietary exposure.’ (Very Limited data available on the use of some substances on some foods.)
 - ‘There is evidence for reduction of pathogens on poultry carcasses and red meats by application of [acidified sodium chlorite] and chlorine dioxide and by application of sodium hypochlorite in smoked fish production. There is some evidence for reduction of cross-contamination by the application of disinfectants (in particular sodium hypochlorite) in wash and flume waters.’

Farmed Salmon & PCBs - 2004

- Hites study (*Science* 303: 226-229) reported higher levels of environmental contaminants, including PCBs, in farmed salmon compared to wild salmon presumably due to contaminants in feed
- Recommended eating farmed salmon no more than 1x /month
- Another highly publicized food scare
- 90 % salmon consumed is farm raised

FDA's Risk Communication - Farmed Salmon/PCBs

- **FDA's advice to consumers is not to alter their consumption of farmed or wild salmon**
- **Fish and shellfish are an important part of a healthy diet. Fish and shellfish contain high-quality protein and other essential nutrients, are low in saturated fat, and contain omega-3 fatty acids.**
- **A well-balanced diet that includes a variety of fish and shellfish can contribute to heart health and children's proper growth and development.**

Risk Communication - Potential Harm?

‘[Academic commenter]...study flawed because it failed to take into account the nutritional benefits of eating salmon. He said any slightly elevated risk of cancer pales in comparison with the advantages of consuming salmon rich with omega-3 fatty acids, which help prevent heart attacks.

Even an increase in farmed salmon consumption, he said, is a worthwhile trade-off in the flight against heart disease, American's No. 1 killer. "I would calculate 6,000 people getting cancer over their lifetime, that's an approximation, versus potentially saving the lives of 100,000 individuals every year.””

LA Times January 9, 2004

Positive Risk Communication

'In the meantime, Eric Rimm of the Harvard School of Public Health in Cambridge, Mass., points out numbers alone may suggest farmed salmon's benefits still outweigh any risk. One in two Americans die every year from cardiovascular disease, while the risk of developing cancer from contaminants remains uncertain and undocumented.'

ABCNews.com January 8, 2004

MeHg – Neurodevelopment Seychelles vs Faroes & New Zealand

- **Faroes: Significant adverse associations, but also beneficial association of fish consumption and some test results; episodic exposure via whale meat and POPs exposure**
- **New Zealand- adverse association (small study; shark)**
- **Seychelles: No consistent impairment; positive effects of omega – 3's appear to be countering MeHg negative effects**

MeHg

Beneficial Effects of Fish and omega-3's

Children

- **Increased IQ**
- **Less risk of lower outcomes for prosocial behavior, fine motor, communication, social development scores**
- **Higher visual acuity**
- **Greater gestational length (one study smaller with oily fish)**
- **Lower risk for preterm delivery and low birth weight**

MeHg

Beneficial Effects of Fish and omega-3's

Adults

- **Reduced stroke – FDA: 20,000 fewer deaths/yr**
 - 27 % lower ischemic stroke risk with fish 1 – 4 x /wk
- **Coronary heart disease-FDA: > 30,000 fewer deaths/yr**
 - Modest fish consumption esp. high in omega-3's: 36% reduction in CHD death
- **Alzheimers risk: 60 % less with ≥ 1 fish meal/wk**
- **Reduced postpartum depression**
- **Reduced preclampsia**
- **Reduced pregnancy anxiety symptoms**

MeHg

U.S. Exposures – Women of Childbearing Age

- Average 1/15th of Seychelles MeHg exposures
- Average 1/10th of Faroes
- Average 1/8th of Japanese women

MeHg

FDA Advisory March 2004 – Do No Harm?

- **Message to Consumers:**

Fish and shellfish are important parts of a healthy and balanced diet. They are good sources of high quality protein and other nutrients. However, depending on the amount and type of fish you consume it may be prudent to modify your diet if you are: planning to become pregnant; pregnant; nursing; or a young child. With a few simple adjustments, you can continue to enjoy these foods in a manner that is healthy and beneficial and reduce your unborn or young child's exposure to the harmful effects of mercury at the same time....

- **Concern that this advisory would contribute to reduced fish consumption and/or below optimal fish consumption**

MeHg

U.S. Exposures – Women of Childbearing Age Where Are We?

- **Oken 2003: Pregnant women cut fish consumption 1/6th (1.4 serv/mo) after the Jan. 2001 fish advisory**
- **Fish consumption women 16 – 49 yr: recommended 8 – 12 oz/wk in 2010 Dietary Guidelines**
 - Mean (308g/30d (2009-10)): 3.5 – 4.7 lower
 - 90th (768g/30d): 1.3 – 1.9 lower
- **2010 Bloomingdale study – pregnant women who ate small amounts of fish, getting advice to limit fish intake, but not being told of the benefits**
- **What about broader consumer confusion on eating fish?**

Inorganic Arsenic (iAs) in Rice

- Lung and Bladder cancer are key endpoints
- Lowest adverse effect level for both: 12.3 $\mu\text{g}/\text{kg}/\text{day}$ (FDA – juice analysis)
- Xue et al (2010) iAs: Total iAs = 0.075 $\mu\text{g}/\text{kg}/\text{day}$
 - Food iAs: 0.05 $\mu\text{g}/\text{kg}/\text{day}$; Water iAs: 0.025 $\mu\text{g}/\text{kg}/\text{day}$
 - Of food: Veg: 24%, Fruit juice/fruit: 18%; Rice 17%; Beer & Wine 12%; Flour, corn & wheat: 11 %
 - Rice 11.3 % of total iAs exposure = 0.0085 $\mu\text{g}/\text{kg}/\text{day}$
- Total iAs exposure 164 x lower than lowest adverse effect & iAs from rice is 1450 x lower
- Mechanism – threshold or not?
- Extrapolation linear or non-linear?

iAs in Rice

Chemical Considerations

- **20 % reduction of iAs in rice results in a trivial ~ 2 % reduction in iAs based on Xue et al., 2010**
- **Avoiding iAs by avoiding rice:**
 - **iAs exposure from other foods like other grains, vegetables**
 - **Exposure to other contaminants:**
 - **Acrylamide from fried potatoes**
 - **Mycotoxins in corn, wheat, barley products**
 - **Perchlorate in vegetables**
 - **Many other possible**

iAs in Rice

Dietary Considerations

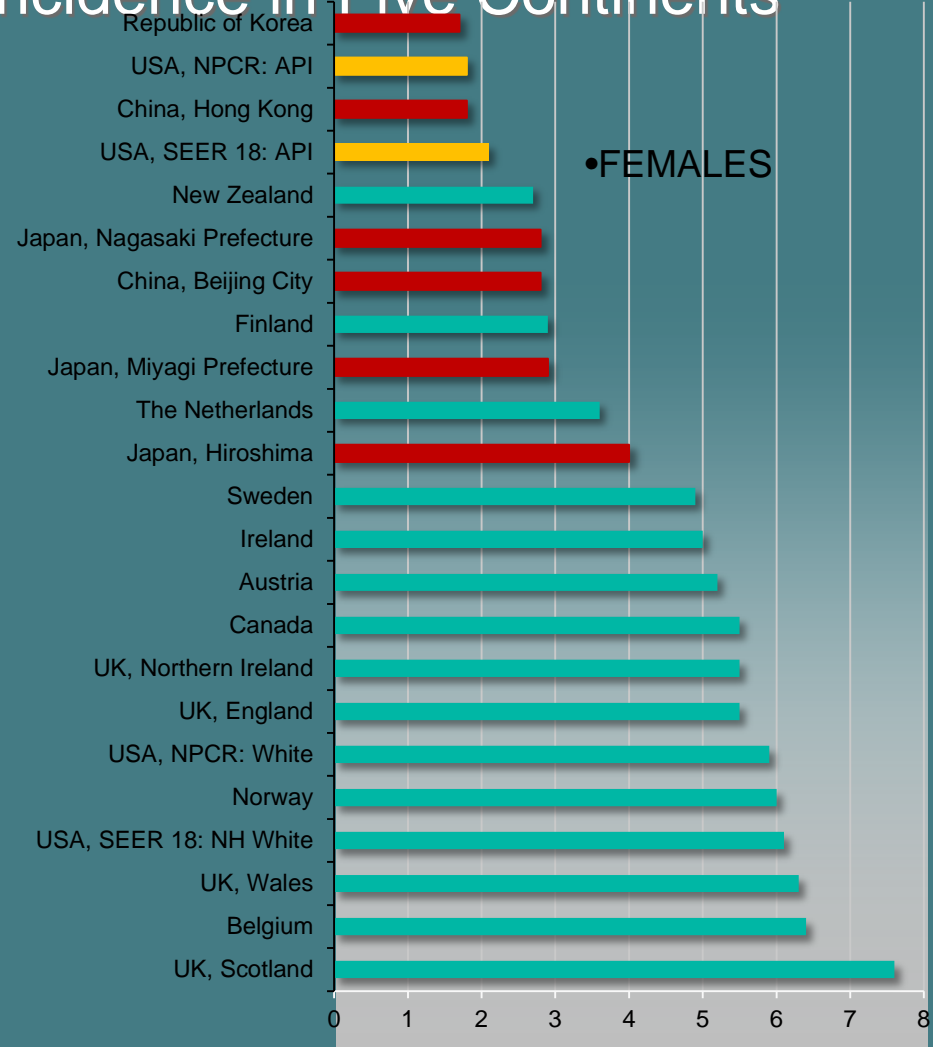
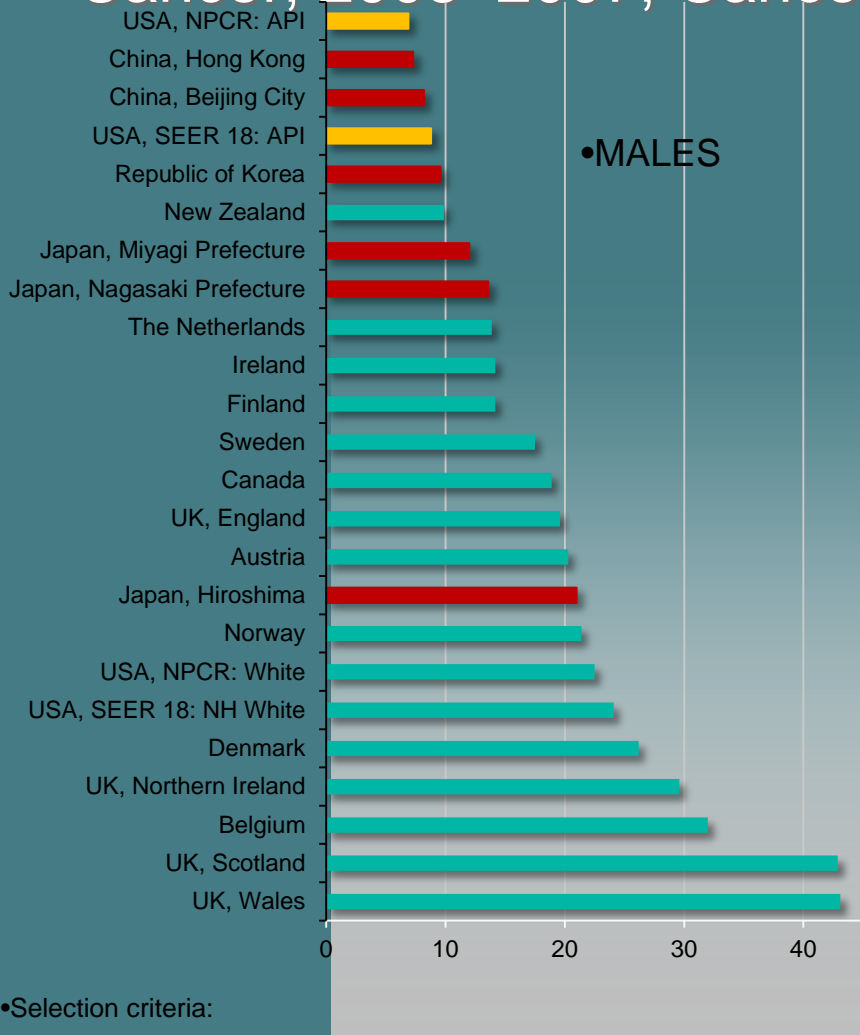
- **Risk of cancer in lifetime: 41% (Am. Cancer Soc.):**
 - actual $R = 0.41$
- **What if estimated iAs risk from rice is 1/10,000?:**
 - Actual risk of cancer 4,100 x greater
- **Peto & Doll (1981) estimated 35% of cancer associated with diet and nutritional practices**
- **Omenn (2011): plausible range 20 – 60 %**
- **What if 30 % of actual cancer associated with diet and obesity?**
 - $R = 0.41 \times 0.3 = 0.12$
 - Actual dietary cancer risk would be 1,200 x greater than hypothetical iAs risk from rice

iAs in Rice

Dietary Considerations

- **Diet related diseases: Deaths (2011 CDC prelim data):**
 - Heart Disease: 598 K
 - Cancer: 575 K
 - Stroke: 129 K
 - Diabetes: 69 K
- **What does this mean?**
- **A very slight shift/perturbation in population diet based on recommendations to avoid a food, or due to fear generated by the media or an advocacy group could result in a larger public health risk than the chemical contaminant of immediate focus.**

Age-standardized (World) Incidence Rates of Bladder Cancer, 2003–2007, Cancer Incidence in Five Continents

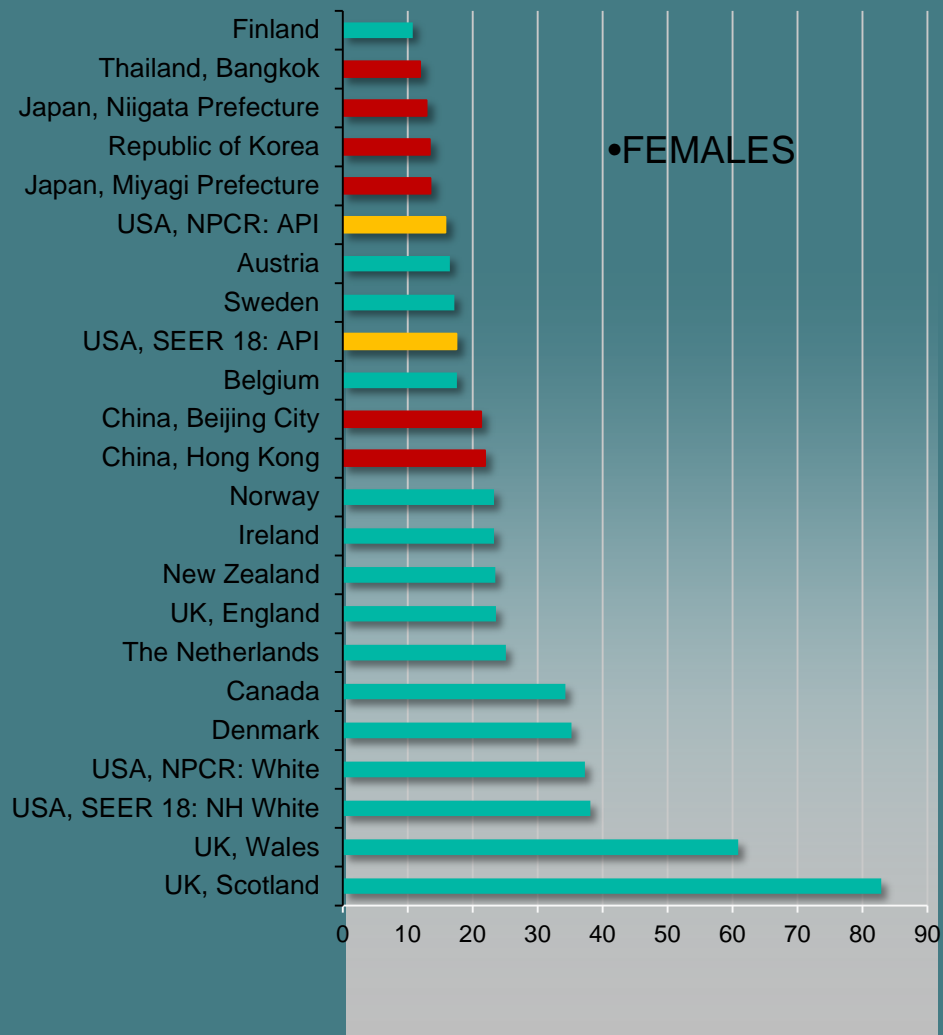
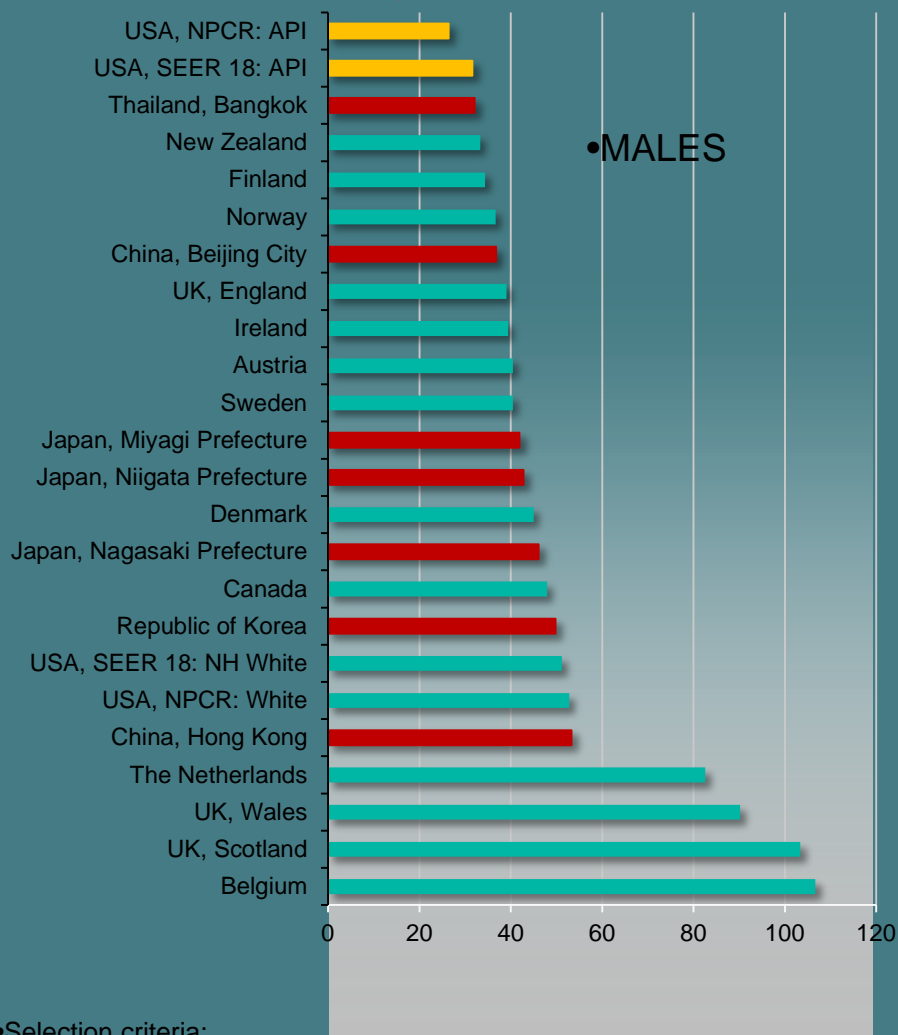


•Selection criteria:

- Europe, North America, and Oceania: national data ([non-Hispanic] Whites and Asians/Pacific Islanders from USA), European countries designated as United Nations "Western Europe and other states," >1000 male/>300 female bladder cancer cases.
- Asia: East/Southeast Asian regions, no asterisk indicating data quality issues, >1000 male/>300 female bladder cancer cases.

- API: Asian/Pacific Islander
- NH: Non-Hispanic
- NPCR: National Program of Cancer Registries
- SEER: Surveillance, Epidemiology and End Results

Age-standardized (World) Incidence Rates of Lung Cancer, 2003–2007, Cancer Incidence in Five Continents



•Selection criteria:

- Europe, North America, and Oceania: national data ([non-Hispanic] Whites and Asians/Pacific Islanders from USA), European countries designated as United Nations "Western Europe and other states," >4000 male/>2000 female lung cancer cases.
- Asia: East/Southeast Asian regions, no asterisk indicating data quality issues, >4000 male/>2000 female lung cancer cases.

•API: Asian/Pacific Islander

•NH: Non-Hispanic

•NPCR: National Program of Cancer Registries

•SEER: Surveillance, Epidemiology and End Results

Rice Health Benefits Study

- Exponent examined literature for white and brown rice separately, whole grains and key nutrients in rice: folate, iron and dietary fiber
- Disease outcomes included: Cardiovascular disease (CVD), obesity, type 2 diabetes, cancer, neural tube defects (NTDs), anemia and mortality
- Rice consumers had significantly higher fiber, iron, folate and whole grain intake than non-rice consumers

Rice Health Benefits Study

- **Exponent compared the diet of consumers in the highest (4th) quartile of rice consumption to the diet in the lowest (1st) quartile and found the following significant health benefits related to the identified dietary component**
- **Brown rice:**
 - **Colorectal polyps: 53 % reduction**
 - **Type 2 Diabetes: 7 % reduction**
- **Folate (females):**
 - **Neural Tube Defect: 28 % reduction**
 - **Incident anemia: 11 % reduction**
 - **Persistent anemia: 21 % reduction**
- **Iron (females):**
 - **Incident anemia: 12 % reduction**
 - **Persistent anemia: 24 % reduction**

Rice Health Benefits Study

- **Dietary Fiber:**

- All cause mortality: 22 – 28 % reduction
- CVD mortality: 22 – 42 % reduction
- Cancer mortality: 15 % reduction (males)
- CVD: 11 % reduction
- Type 2 Diabetes: 16 % reduction
- Colorectal cancer: 7 % reduction
- Obesity: 32 % reduction

- **Whole Grains:**

- Obesity: 22 % reduction (females)
- Type 2 diabetes: 37 % reduction
- CVD: 18 % reduction

Rice Health Benefits Study

- Even though the US is generally not a high rice consuming country, diets of US consumers that eat more rice are associated with significant health benefits.
- This further supports the concern that any slight shift in these dietary patterns may result in greater harm than any tiny reduction in the iAs risk

Summation

- **Protecting the public health is paramount**
- **Do No Harm:**
 - Imperative that risk managers consider consequences of any proposed policy for a specific chemical contaminant
 - Nutrient/obesity risks from dietary shifts resulting from a chemical contaminant concern may far exceed any chemical risk reduction; and messaging to prevent the dietary risk is difficult and may not be possible.
 - The media as do advocacy groups have a tremendous responsibility to not increase the public health hazard by over emphasizing the potential health risks.
- **Truth:**
 - The lack of knowledge of actual chemical risk likely exaggerates predicted risk reductions resulting in the potential to ‘do harm’ in any risk management action
 - Research is needed to more precisely define all the risks that will be incurred in a risk management action

Acknowledgements

- **Paige Miller and Leila BarraJ were primarily responsible for the benefits analysis for rice that was supported by the Rice Foundation**
- **The world cancer incidence slides for lung and bladder cancer were developed by Joyce Tsuji and her group**