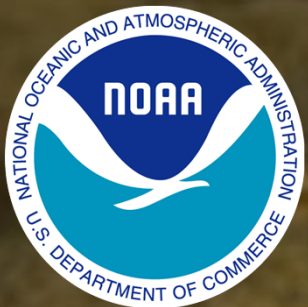


Contaminants of Emerging Concern in Puget Sound (Drugs in Salmon)



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Contaminants of Emerging Concern (CECs)

All poorly studied

Pharmaceuticals

Antibiotics, Antifungals
Analgesics, Sedatives, Blood pressure
Antidepressants (Prozac)
Corticosteroids, Hormones
Metabolic regulators



Personal care products

Surfactants (soaps and detergents)
Sunscreens, Insect repellants
Synthetic musks, Preservatives
Perfume, Lotions



Other compounds

Nicotine, Caffeine & metabolites
Illicits
Flame retardants (PBDEs)
Bisphenol A, Phthalates
Nonylphenol



Wastewater Chemicals

Pharm & Personal Care Products

Acetaminophen
Ampicillin
Azithromycin
Caffeine
Carbadox
Carbamazepine
Cefotaxime
Ciprofloxacin
Clarithromycin
Clinafloxacin
Cloxacillin
Dehydronifedipine
Digoxigenin
Digoxin
Diltiazem
1,7-Dimethylxanthine
Diphenhydramine
Enrofloxacin
Erythromycin-H2O
Flumequine
Fluoxetine
Lincomycin
Lomefloxacin
Miconazole
Norfloxacin
Norgestimate
Ofloxacin
Ormetoprim
Oxacillin
Oxolinic acid
Penicillin G
Penicillin V
Roxithromycin
Sarafloxacin

Sulfachloropyridazine
Sulfadiazine
Sulfadimethoxine
Sulfamerazine
Sulfamethazine
Sulfamethizole
Sulfamethoxazole
Sulfanilamide
Sulfathiazole
Thiabendazole
Trimethoprim
Tylosin
Virginiamycin
Bisphenol A
Furosemide
Gemfibrozil
Glipizide
Glyburide
Hydrochlorothiazide
2-OH-ibuprofen
Ibuprofen
Naproxen
Triclocarban
Triclosan
Warfarin
Albuterol
Amphetamine
Atenolol
Atorvastatin
Cimetidine
Clonidine
Codeine
Cotinine
Enalapril
Hydrocodone
Metformin

Oxycodone
Ranitidine
Triamterene
Alprazolam
Amitriptyline
Amlodipine
Benzoyllecgonine
Benzotropine
Betamethasone
Cocaine
DEET
Desmethyldiltiazem
Diazepam
Fluocinonide
Fluticasone
Hydrocortisone
10-OH-amitriptyline
Meprobamate
Methylprednisolone
Metoprolol
Norfluoxetine
Norverapamil
Paroxetine
Prednisolone
Prednisone
Promethazine
Propoxyphene
Propranolol
Sertraline
Simvastatin
Theophylline
Trenbolone
Valsartan
Verapamil

Hormones

Allyl Trenbolone
Androstenedione
Androsterone
Desogestrel
Estriol
Mestranol
Norethindrone
Norgestrel
Progesterone
Testosterone
17 α -Dihydroequilin
Equilenin
Equilin
17 α -Estradiol
17 β -Estradiol Estrone
17 α -Ethinylestradiol

Perfluorinated compounds

Perfluorooctanoate (PFOA)
Perfluorononanoate (PFNA)
Perfluorodecanoate (PFDA)
Perfluorodecanoate (PFUnA)
Perfluorohexanesulfonate (PFHxS)
Perfluorooctanesulfonate (PFOS)
Perfluorooctane sulfonamide (PFOSA)

Alkylphenols and alkylphenol ethoxylates

Nonylphenol (NP)
4-Nonylphenol monoethoxylate (NP1EO)
4-Nonylphenol diethoxylate (NP2EO)
Octylphenol (OP)

Phthalate ester metabolites

Mono-methyl phthalate
Mono-ethyl phthalate
Mono ethylhexyl phthalate
Mono-butyl phthalate
Mono-(3-carboxypropyl) phthalate

Flame retardants

Alpha-Hexabromocyclododecane
Beta-Hexabromocyclododecane
Gamma-Hexabromocyclododecane

4,000 pharmaceuticals available – 1,100 unique

Found in water and tissue
Found in water only

Puget Sound study site



Sinclair: outfall 10 m

Puyallup: outfall 40 m

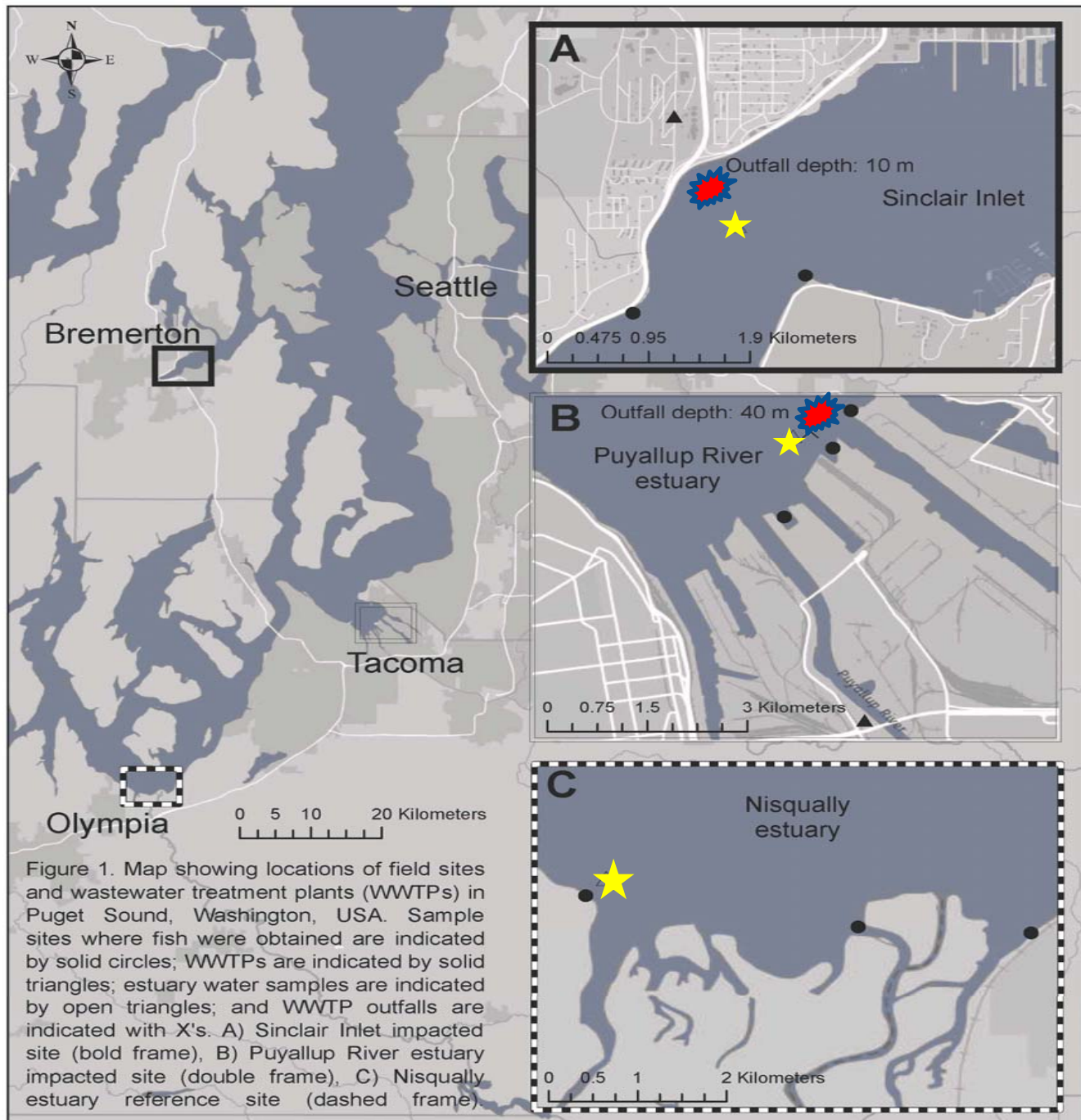
Nisqually: Reference site



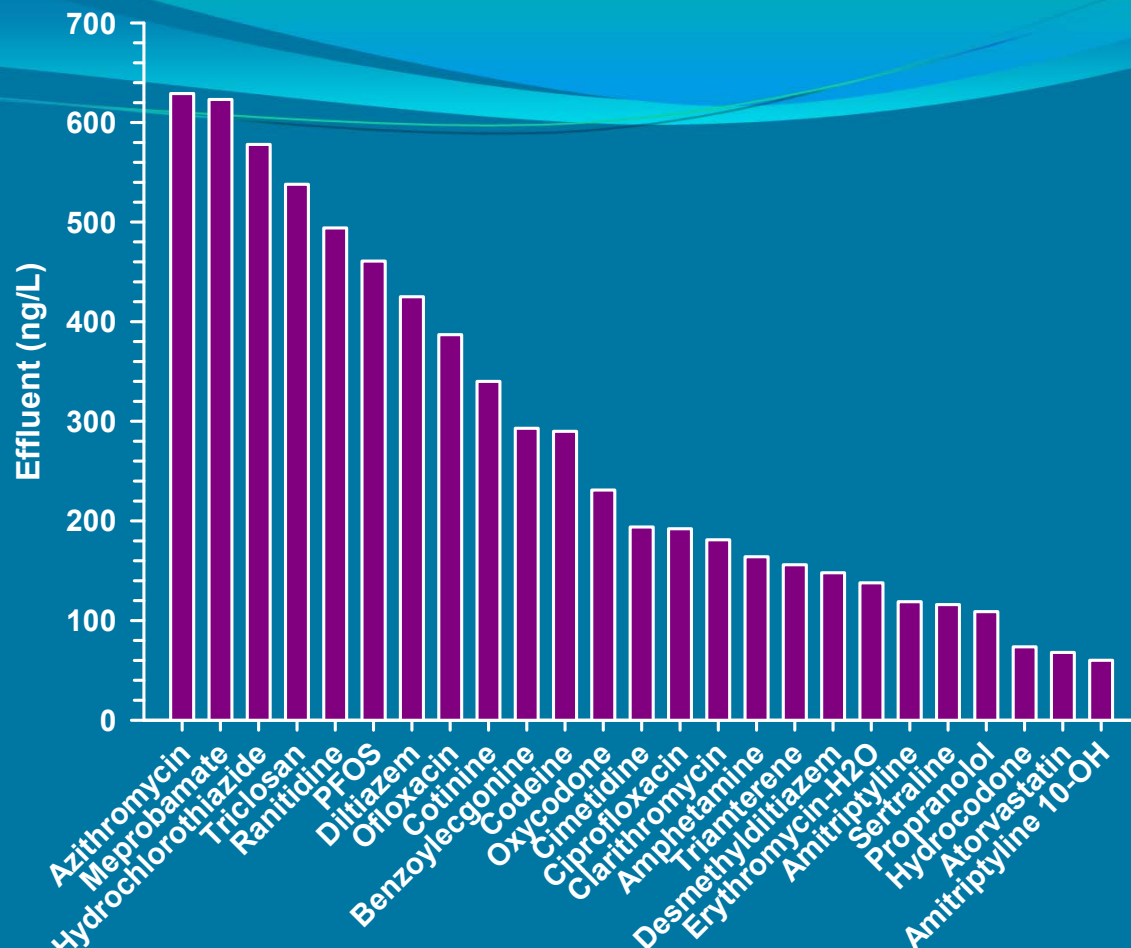
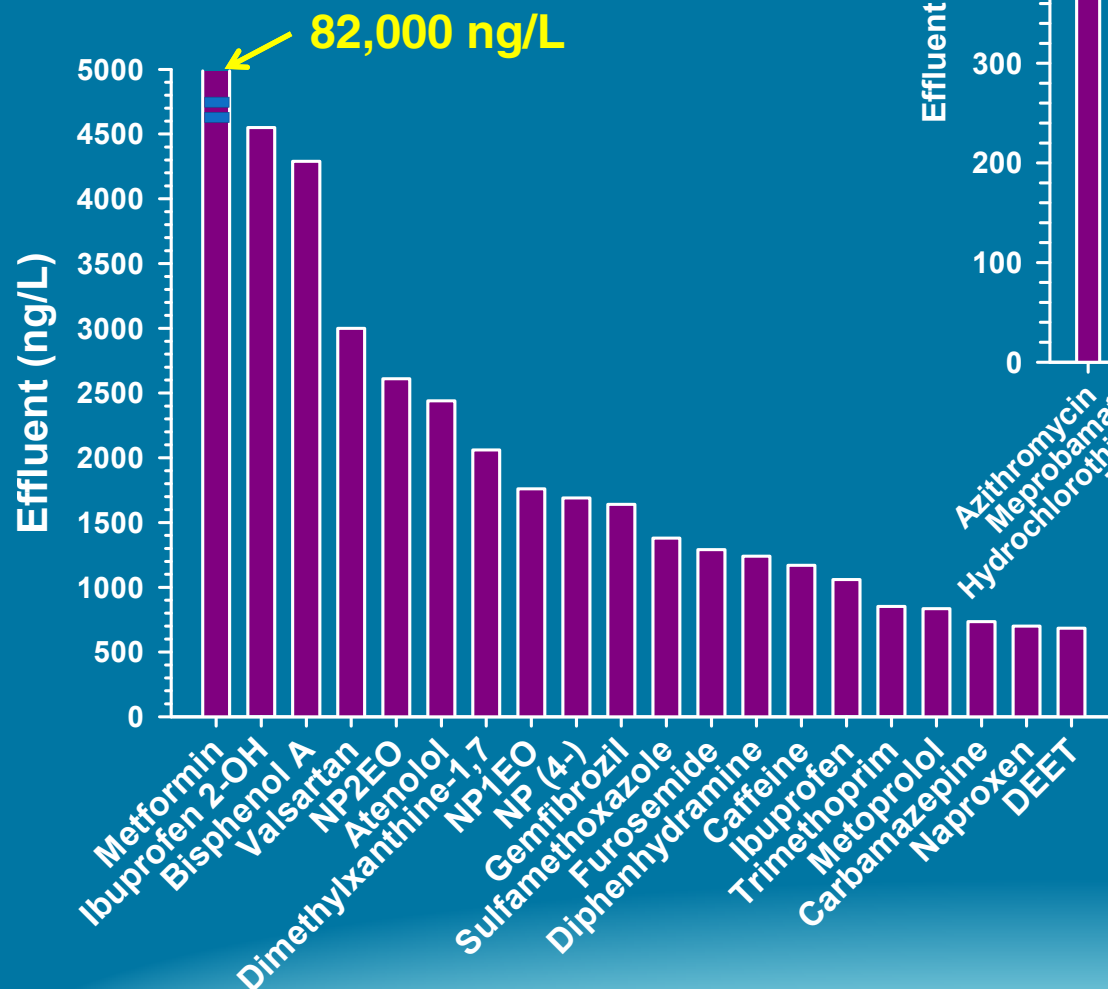
Water samples at 2 m



Fish collection



WWTP effluent concentrations

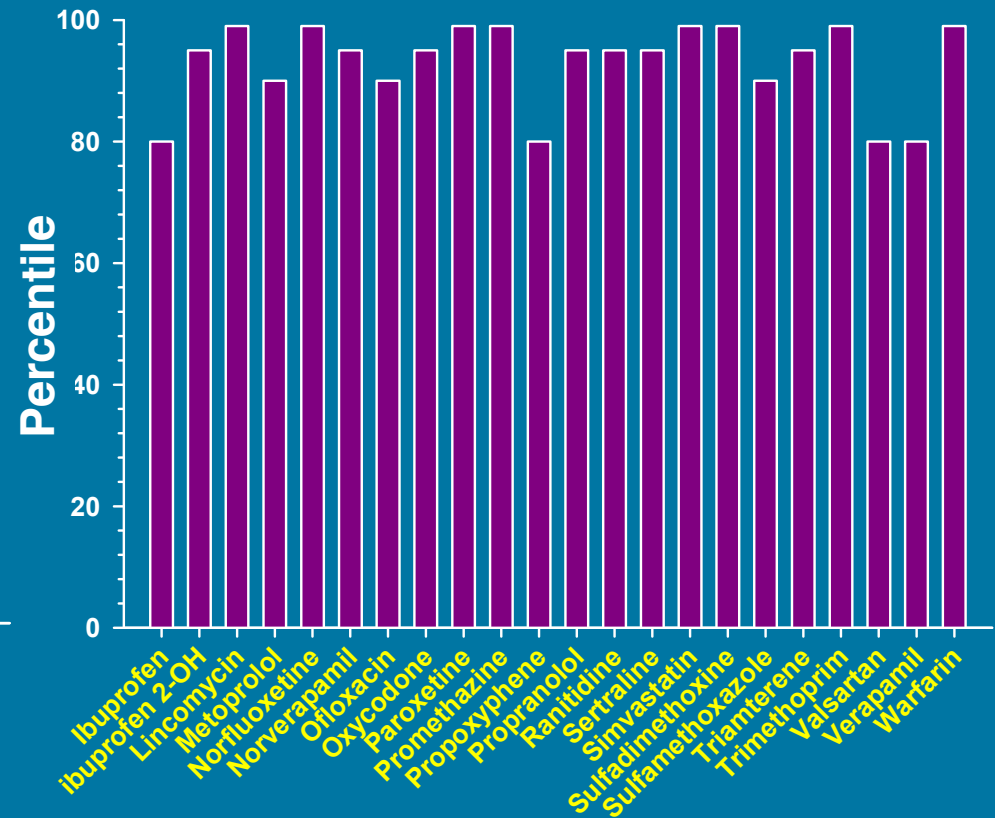
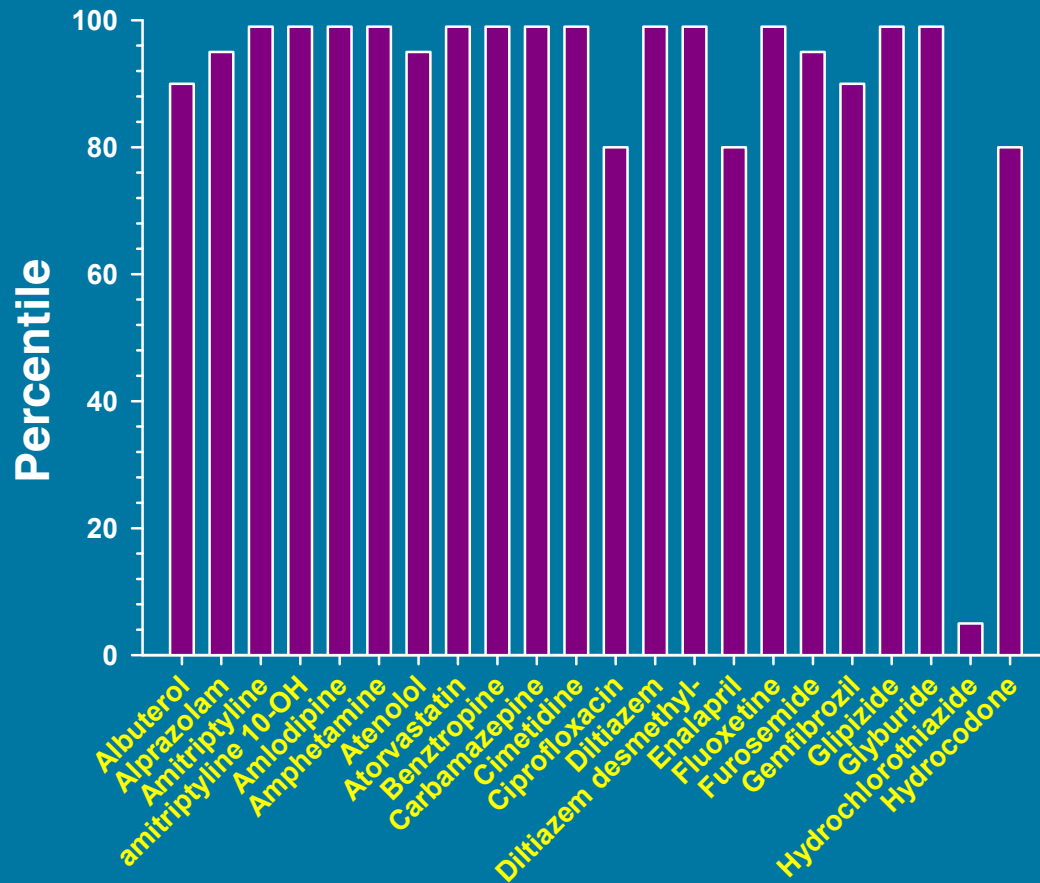


+ 36 additional chemicals detected (not shown) – 2 to 50 ng/L

81 chemicals (54%) detected

Percentile ranking for effluent concentrations

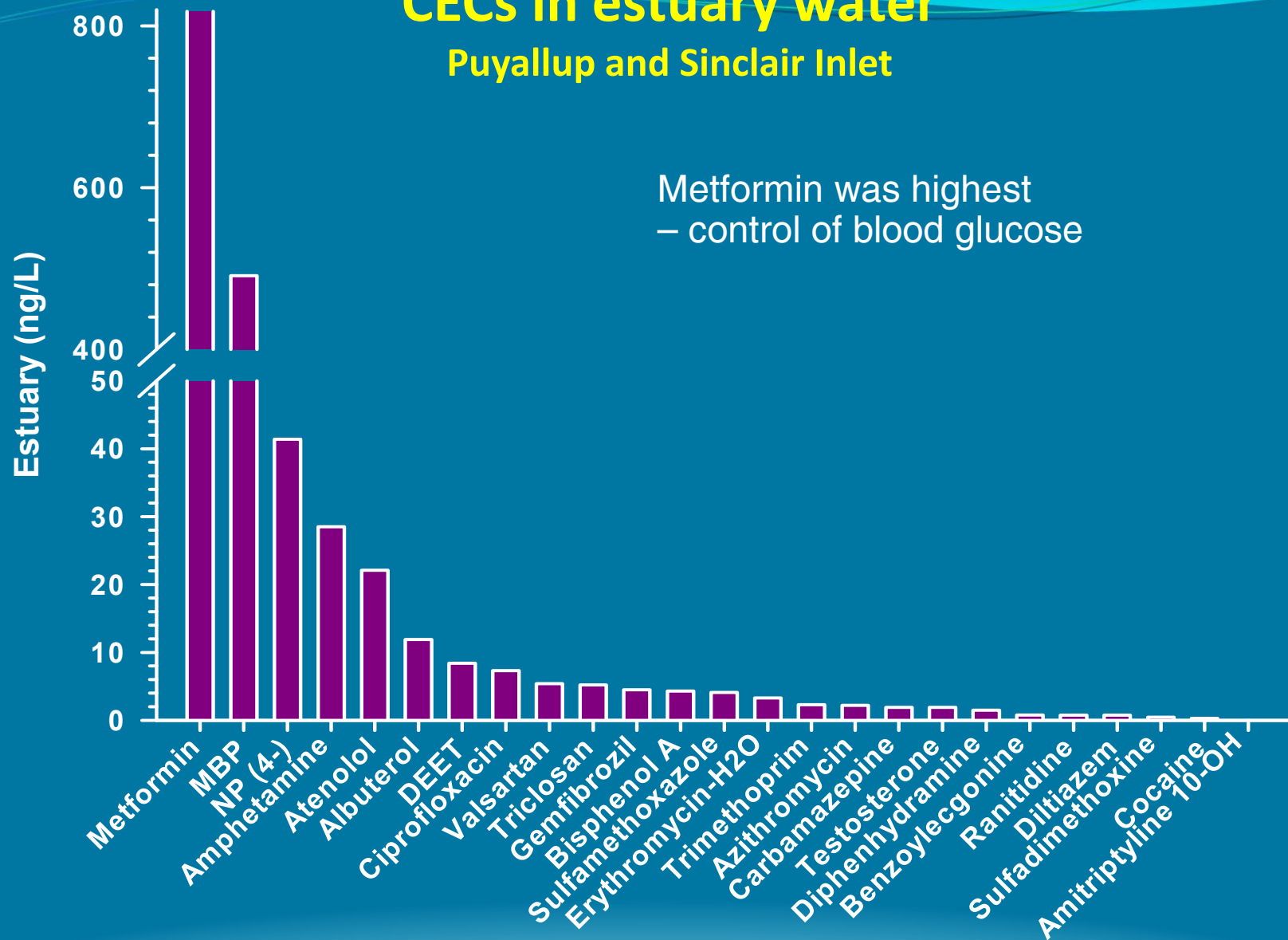
compared to Kostich et al. 2014 (EPA)



Puget Sound effluent compared to effluent observed in 50 largest WWTPs in U.S.

CECs in estuary water

Puyallup and Sinclair Inlet



Wastewater Outfalls Puget Sound

Total inputs from wastewater treatment plants (WWTP)

103 WWTPs Puget Sound - 336 MGD
(million gallons per day)

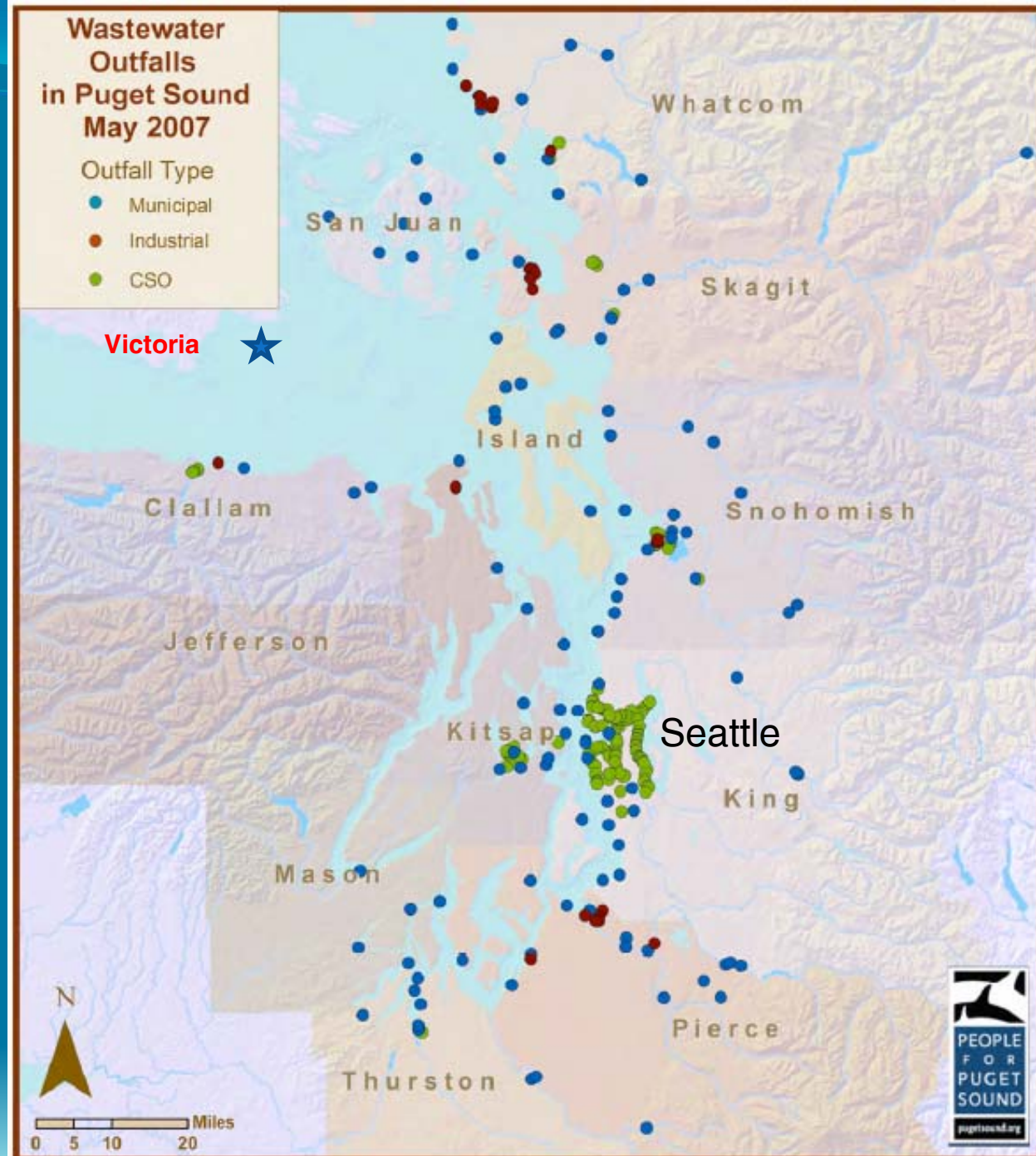
Tacoma WWTP – 15.1 lb / day
Bremerton WWTP – 1.8 lb / day

≈ 266 lb / day or ≈ 100,000 lb / yr

Not including – leaky septics and unmeasured chemicals

Low concentrations add up to big inputs! It's all about volume.

Is this a big number? Don't know!



CECs in staghorn sculpin

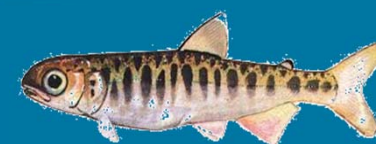


Class	CEC	ng / g
Anti-anxiety	Diazepam	0.3
	Alprazolam	0.4
Antibiotics	Ciprofloxacin	16.6
	Virginiamycin M1	33.9
Antidepressants	Amitriptyline 10-OH	0.1
	Sertraline	0.2
Antihistamines	Diphenhydramine	0.3
	Ranitidine	0.97
Glucose	Metformin	27.8

Class	CEC	ng / g
Ca channel blockers	Diltiazem desmethyl	0.08
	Norverapamil	0.3
	Verapamil	0.3
Industrials	Bisphenol A	4.5
	4-NP	35.2
	NP1EO	4.9
	NP2EO	16.5
	PFDA	0.8
Insect repellants	DEET	2.2
Stimulants	Amphetamine	7.5
	Caffeine	12.9

CECs in juvenile Chinook salmon

42 chemicals detected



Class	CEC	ng / g
Anti-anxiety	Diazepam	0.4
Antibiotics	Azithromycin	1.7
	Erythromycin	0.9
	Miconazole	1.8
	Ormetoprim	1,600
	Sulfadiazine	0.9
	Sulfadimethoxine	16.8
	Sulfamerazine	0.5
	Triclocarban	6.5
	Triclosan	26.4
	Virginiamycin M1	10.2
Antidepressants	Amitriptyline 10-OH	0.1
	Amitriptyline	0.7
	Fluoxetine	4.9
	Norfluoxetine	3.2
	Sertraline	17
Antihistamines	Diphenhydramine	2.7
	Ranitidine	1.1
Blood pressure	Enalapril	1.2

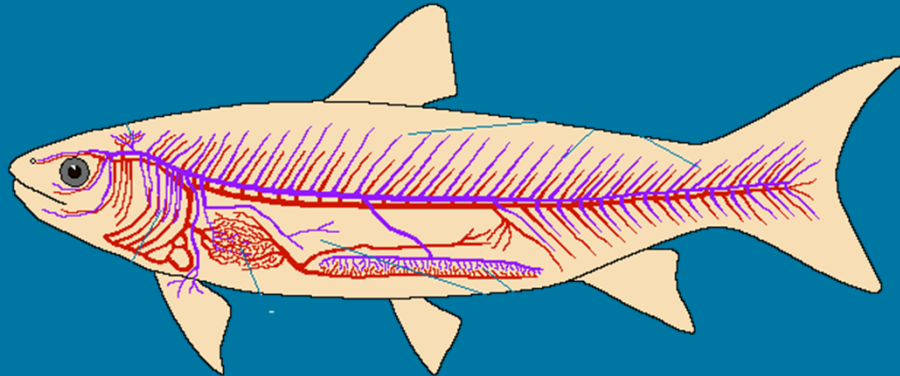
Class	CEC	ng / g
Ca channel blockers	Amlodipine	1.0
	Diltiazem	1.6
	Diltiazem desmethyl	1.5
	Norverapamil	0.5
	Verapamil	0.6
Glucocorticoids	Fluocinonide	6.5
Industrials	Bisphenol A	40.7
	α HBCDD	0.2
	γ HBCDD	0.4
	4-Nonylphenol	75.6
	Nonylphenol-1EO	60
	Nonylphenol-2EO	51
	PFDA	0.8
	PFOS	33.7
Insect repellants	DEET	1.6
Metabolic	Gemfibrozil	1.3
	Metformin	27.8
Stimulants	Amphetamine	24.5
	Caffeine	18.3
Parkinsons	Benzotropine	0.2

Potential effects for fish from CEC exposure

	Observed concentrations				Toxic concentrations		
Class	CEC	Eff ng / L	Est ng / L	Tiss ng / g	Water ng / L	Tissue ng / g	Response
Antibiotics (-mycins and sulfa drugs)	6 compounds	979	5.5	13 - 34	?	?	Affect natural bacteria & ↑pathogenic bacteria
Hormones	Estrone (E1)	58			15 - 54		Endocrine disruptor
	Testosterone		1.9				Endocrine disruptor
Anti-depressants	Fluoxetine (Prozac)	60	-	4.9	28	0.17 brain	↑Mort, ↓aggression, Endocrine disruptor
	Norfluoxetine	28	-	3.2	≈ to fluoxetine		
	Sertraline	116	-	17	16 – 52	0.06 brain	
Metabolic regulators	Metformin	82,700	832	27.8	40,000		↓growth
Personal care products	Triclosan	538	5.2	26.4	560		↑aggression, Endocrine disruptor
	Triclocarban	17	-	6.5	179		
Industrial	Nonylphenol	1690	41	75	1,700 (EPA WQC)		↓growth, ED
	Nonylphenol EO1	1760		59	850		↓growth, ED
	Nonylphenol EO2	2610		41	850		↓growth, ED

Mixture effects?

Fish Plasma Model

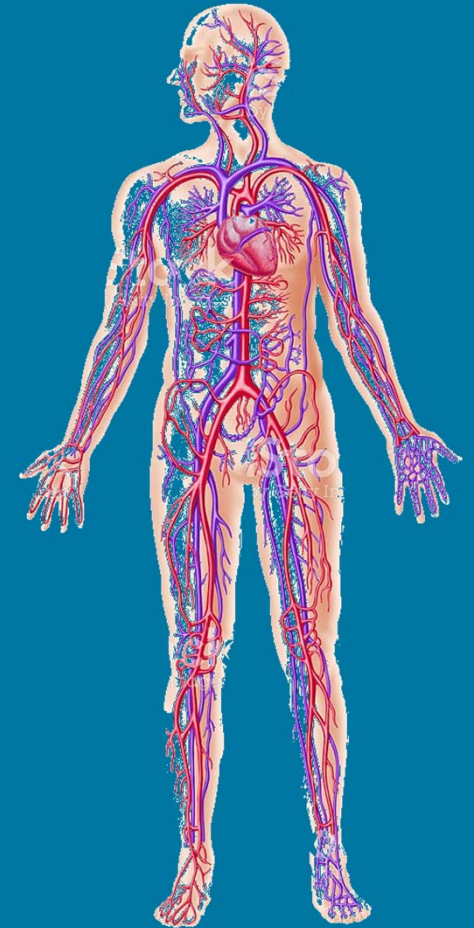


Concentration of pharmaceutical in human plasma compared to that in fish - used to estimate effects

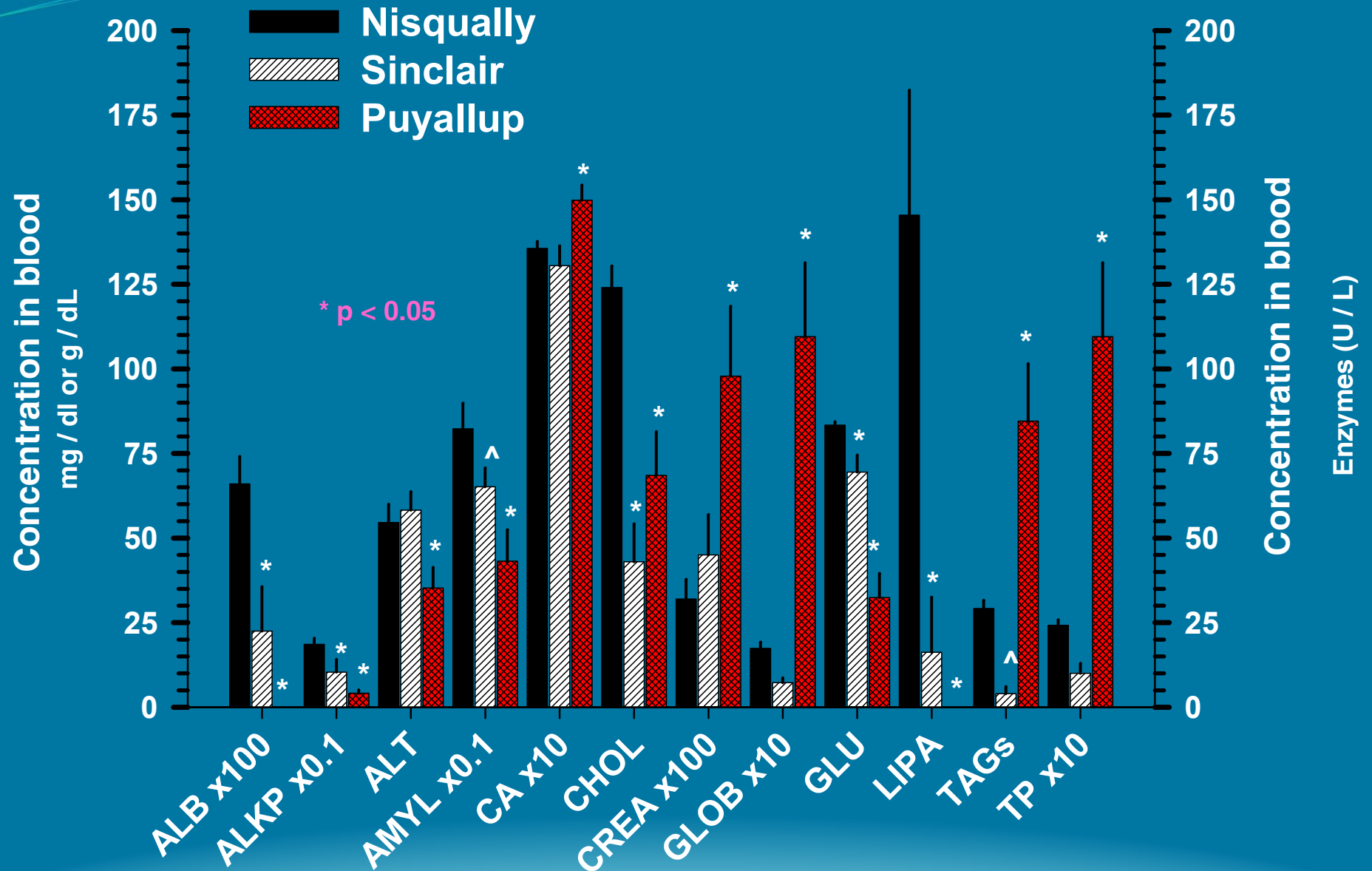
Database of human C_{max} values = Max concentration resulting in **therapeutic** effect

Therapeutic effect for humans $\neq$ beneficial effect for fish

1318 human drug targets - 86% very similar in fish



Plasma chemistry - juvenile Chinook

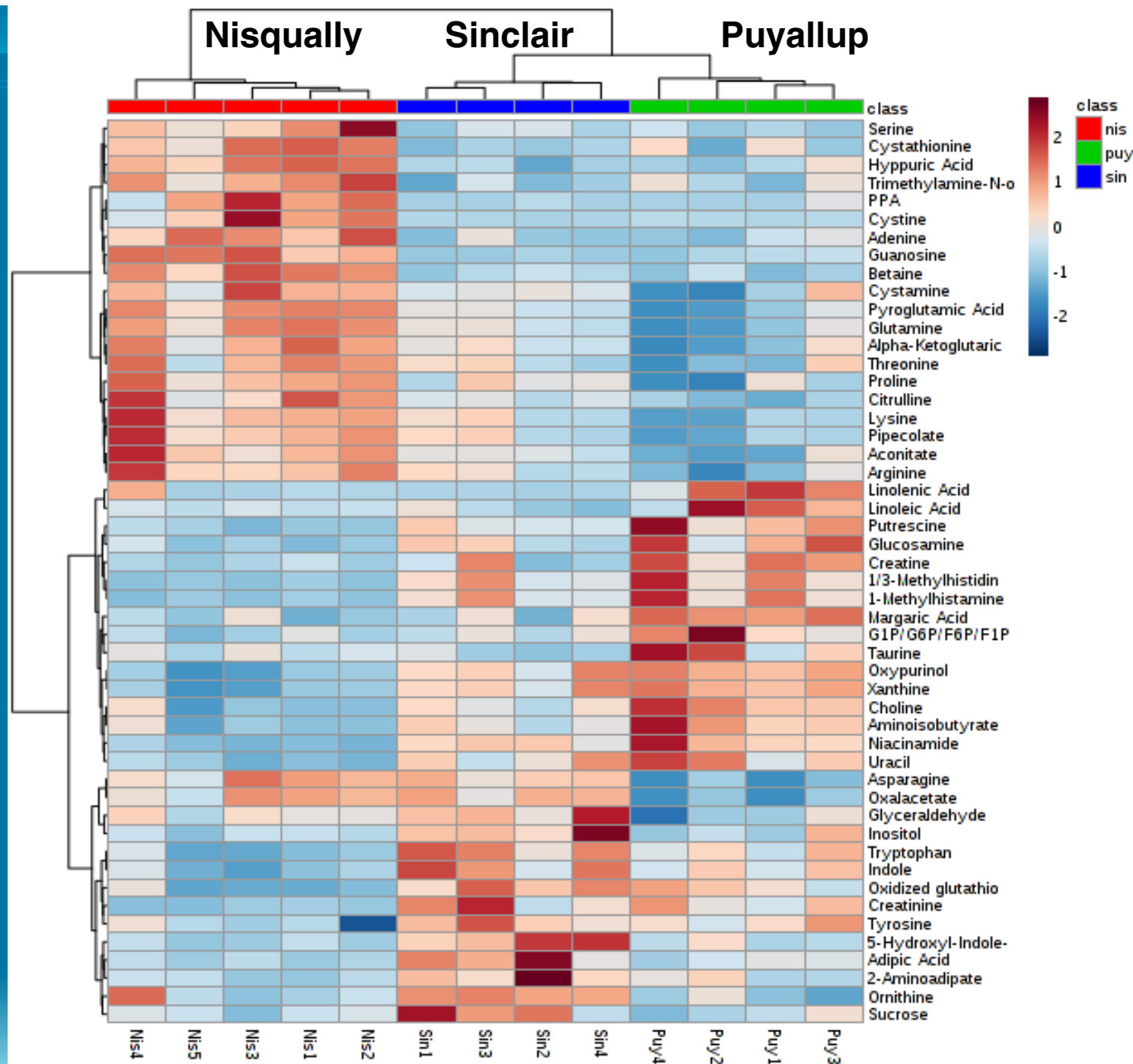


Targeted Metabolomics Plasma from juv. Chinook

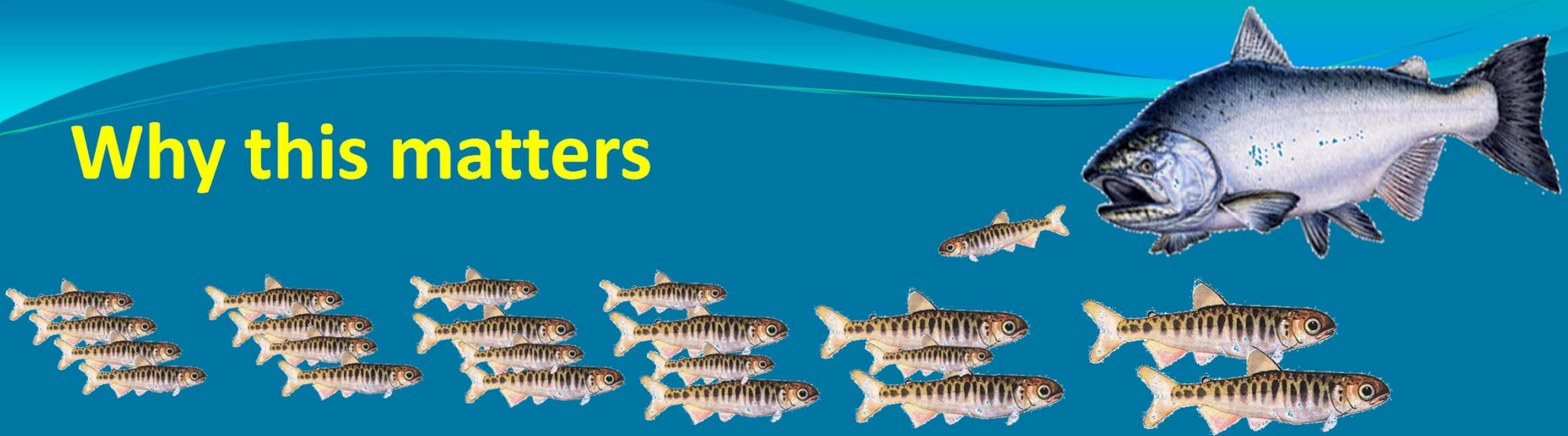
Heatmap (40 significant)

Red = higher
Blue = lower

Each column
is one composite
sample of several
fish



Why this matters



Growth and behavior

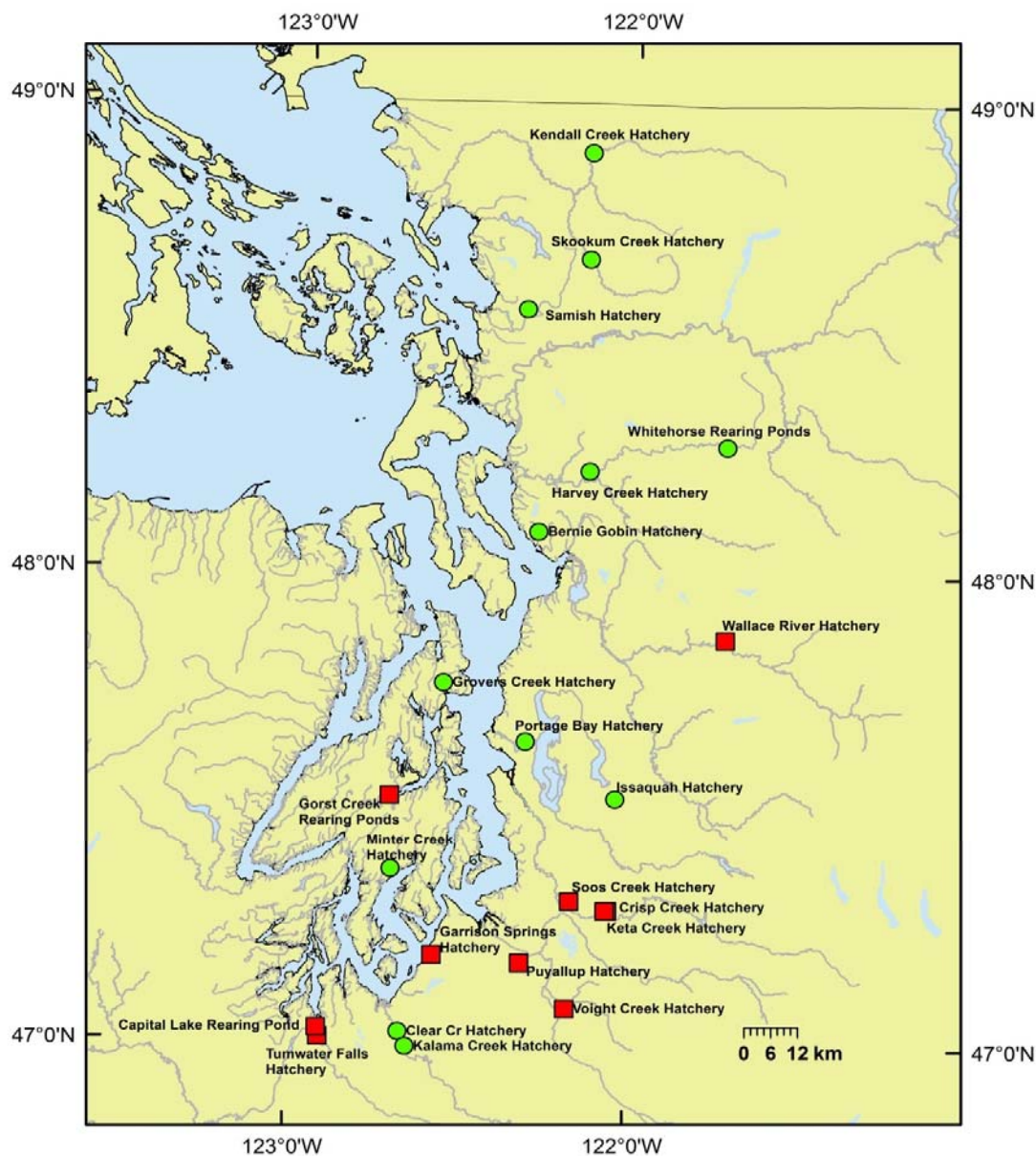
- Small fish and those behaving oddly have higher probability of being eaten. Juvenile Chinook salmon can grow 3 – 5% / day

Lipid storage

- Juvenile salmon need a certain level of stored lipid to survive winter

Contaminants from wastewater

- Are known to affect growth, behavior, and basic metabolism



Salmon Survival in Local Estuaries

- 22 hatcheries
- 14 Local estuaries
- 8 Clean & 6 Contaminated estuaries
- 36 years of data (1972 – 2008)
- Many estuaries with WWTPs

Average survival for Chinook salmon

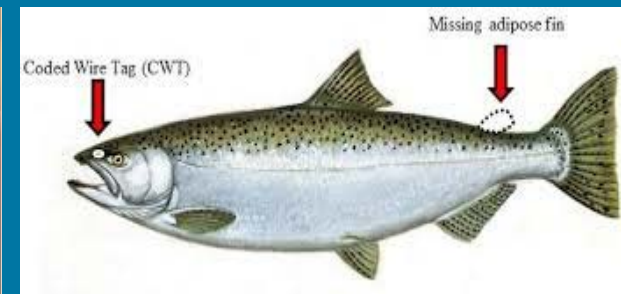
Contaminated estuaries = **0.48%**

Uncontaminated estuaries = **0.87%**

Survival almost 2x higher in clean estuaries

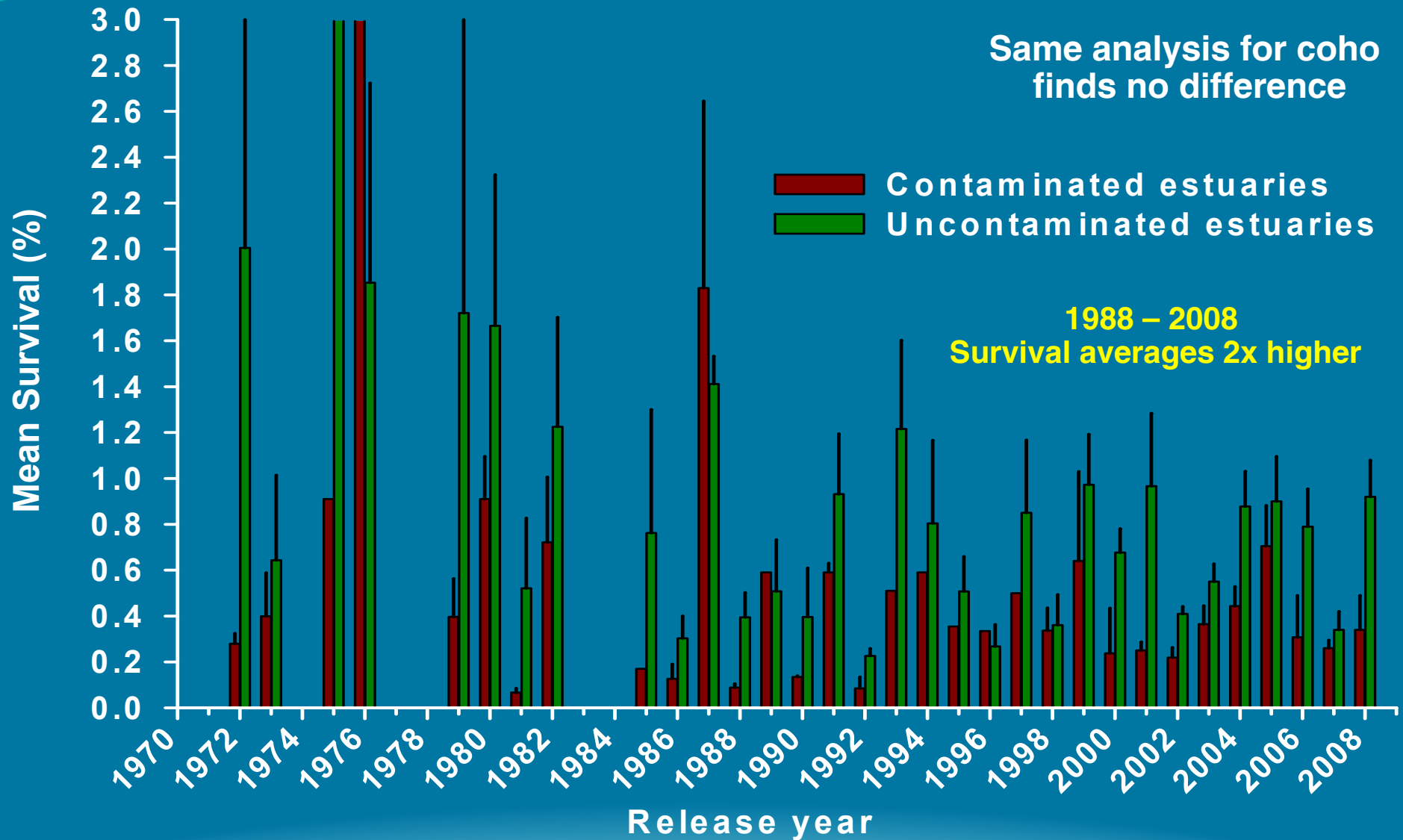


Coded wire tag



Pacific States Marine Fisheries Commission

Chinook data - all years (n = 32)



Toxic Mixtures



What other drugs will affect Zoloft?
Taking Zoloft with other drugs that make you sleepy or slow your breathing can increase these effects. Ask your doctor before taking Zoloft with a sleeping pill, narcotic pain medicine, muscle relaxer, or medicine for anxiety or seizures.



What other drugs will affect Metformin?

Tell your doctor about all other medicines you use, especially:

Lasix; Adalat, Procardia, Tagamet, Zantac, Midamor, Dyrenium, Lanoxin, MS Contin, Kadian, Oramorph, Procan, Pronestyl, Procanbid. Quin-G, quinine, Proloprim, Primsol, Bactrim, Cotrim, Septra, Vancocin, Lyphocin).



Fish don't have a choice!

Open for questions!

