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One Health Approach for Evaluating Risks of Pharmaceuticals Discharged via a Norwegian Wastewater Treatment Plant in the Marine Environment

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ONE HEALTH: A JOINT SETAC/ACES SESSION ON THE INTERFACE OF ECOSYSTEM TOXICOLOGY AND SERVICES | 11 DECEMBER 2024 | AUSTIN, TEXAS

Case scenario: The wastewater discharge of Stavanger, the 4th largest city in Norway

The wastewater treatment plant (WWTP) (certified ISO standards NS-EN ISO 9001: 2015 (quality) and NS-EN ISO 14001: 2015 (environment) have been developed to remove (and recycle) biodegradable carbon and nutrients, using secondary wastewater treatment processes.

It serves a population equivalent of 400 000 and various activities (domestic and industrial, including university hospital)

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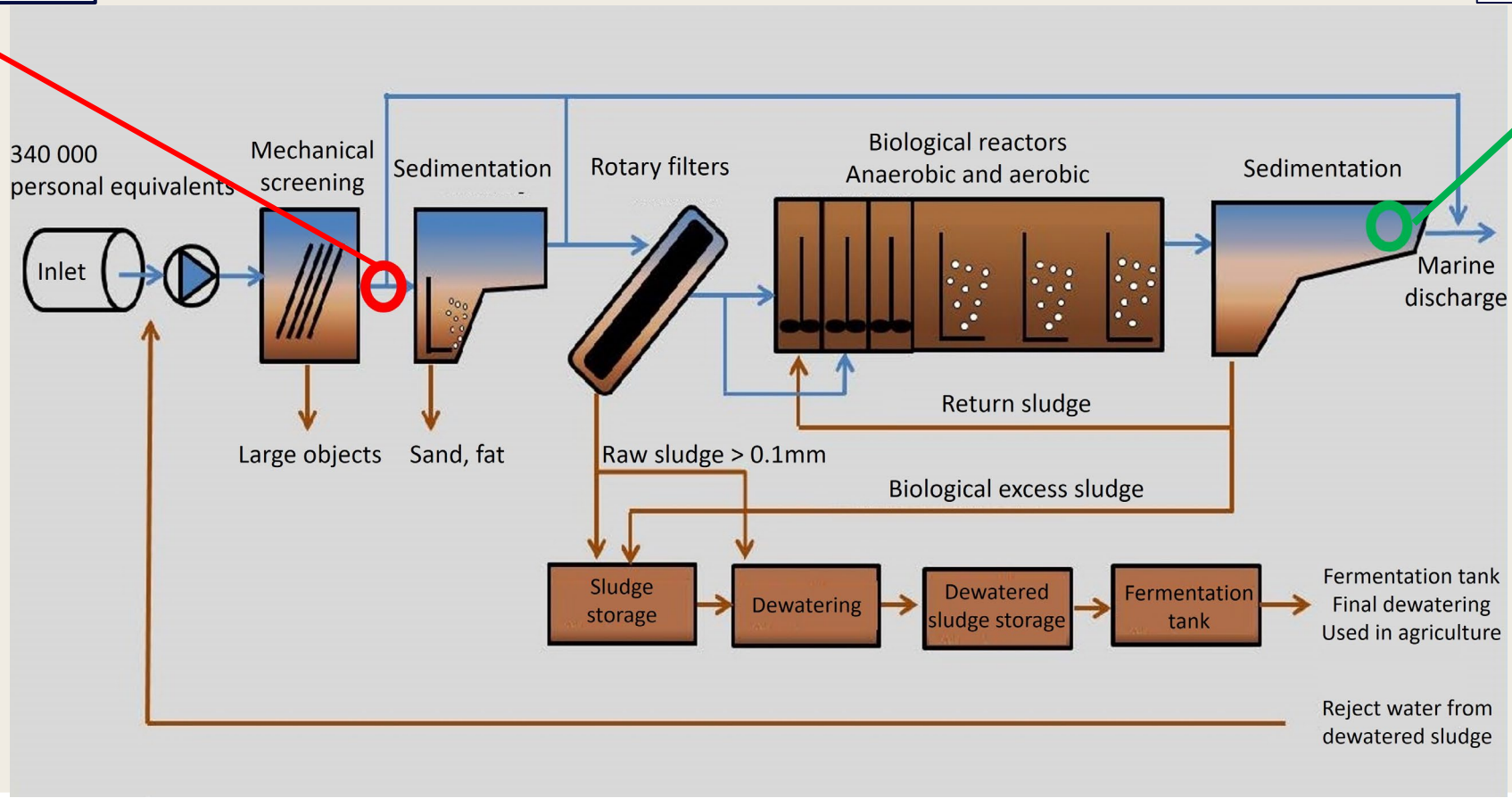
Wastewater Treatment Plant of Stavanger

Sample collection

INFLUENT

EFFLUENT



I L composite
3 x hr
MeOH/H2SO4

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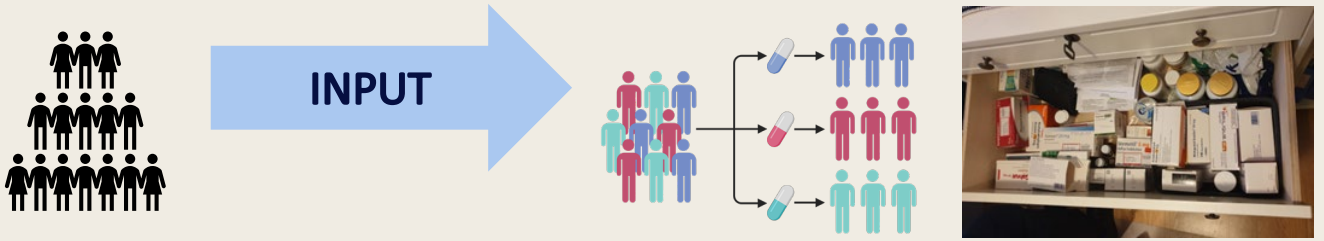
Selection of targeted PPCPs based on prescription and sales of over-the-counter



The most traded active substances reported as defined daily doses (DDD)

Rank	Active ingredient	Increase 2020-2021 (%)	Therapeutic group	Use
1	Atorvastatin	9,6	Lipid regulator	High colesterol
2	Acetylsalicylic Acid	-1,9	Nonsteroidal anti-inflammatory drug (NSAID)	Blood clot
3	Paracetamol (Acetaminophen)	5,4	Analgetic	Pains
4	Candesartan	8,1	Angiotensin receptor blocker	High blood pressure
5	Xylometazolin	7,0	Decongestant	Stuffy nose
6	Amlodipine	3,8	Antihypertensive (Beta blocker)	High blood pressure
7	Cetirizine (Zyrtec)	2,9	Antihistamine	Allergy
8	Desloratadine	12,2	Antihistamine	Allergy
9	Cholecalciferol (Vitamin D3)	21,7	Dietary supplement	Dietary supplement
10	Esomeprazole	6,0	Proton pump inhibitor	Gastroesophageal reflux

PPCPs in influent and effluent of the WWTP

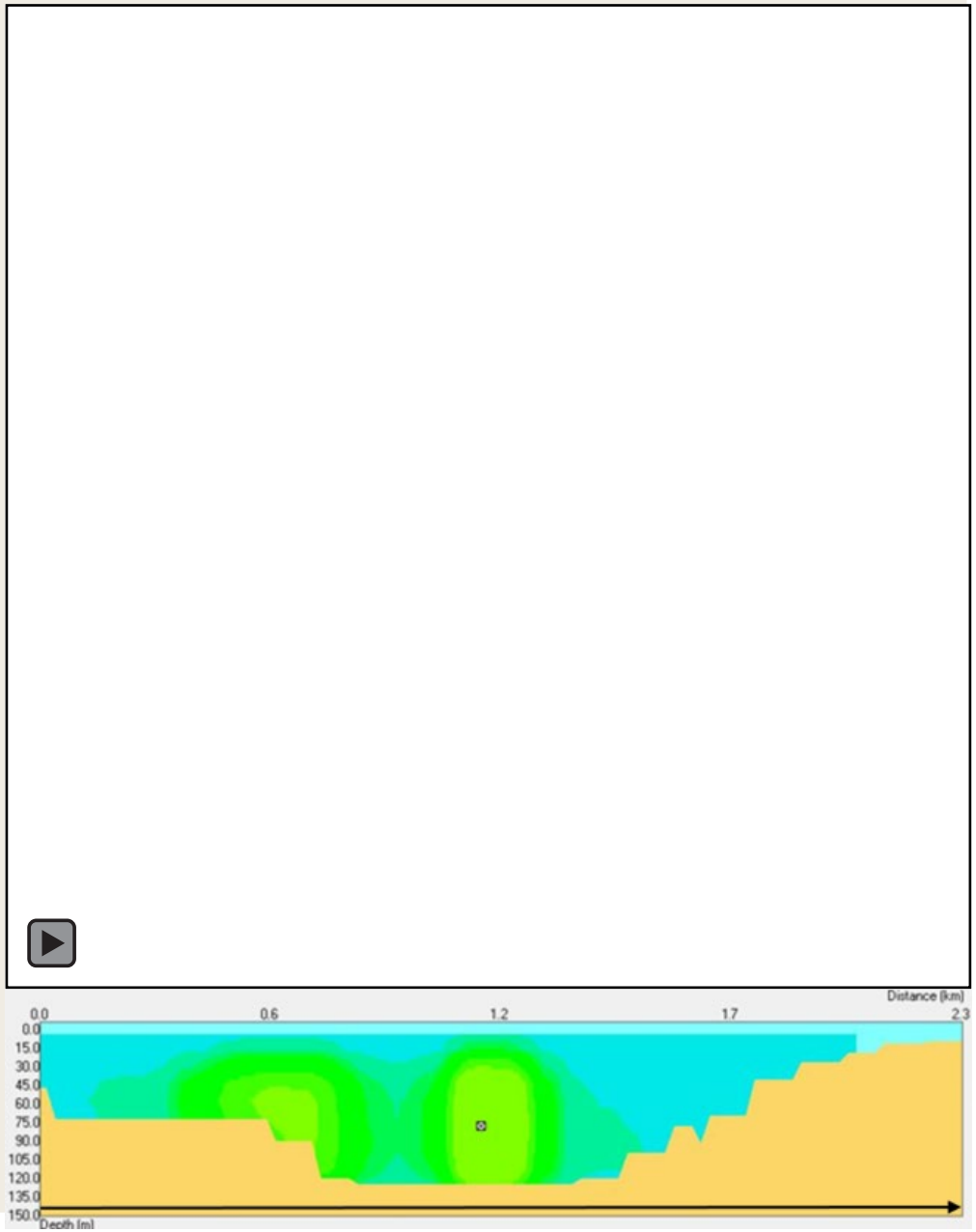
Abbreviation	Name	Therapeutic group	Influent (ng/L)	Effluent (ng/L)	Removal (%)	PNEC (µg/L)
ACE	Acetaminophen	NSAID	83.00	<LOD	98	
ACR	Acridine	Topical antiseptic	<LOD	<LOD	-	
AMT	Amitriptylene	Antidepressant	4.93	6.24	-27	0.13576
ATE	Atenolol	Antihypertensive (beta blocker)	113.80	0.60	99	150
ATORVA	Atorvastatin	HMG-CoA reductase inhibitors (statins)	682.30	<LOD	100	
ATZ	Atrazine	Herbicide	21.76	<LOD	99	
BTA	Benzotriazole	Antimicrobial activity	430.27	10.89	97	19
MBTA	Methyl-1H-benzotriazole	Anti-icing fluids/detergent/building block for UV absorbers	339.90	5.50	98	150
CAF	Caffeine	Stimulant	48066.47	69.94	100	0.1
CBZ	Carbamazepine	Antiepileptic	75.92	66.92	12	2
CBZ-EPO	Carbamazepine-10,11-epoxide	Antiepileptic	<LOD	<LOD	-	
CPM	Chlorphenamine	Antihistamine	0.67	<LOD	87	
CIP	Ciprofloxacin	Antibiotics	16.57	7.88	52	0.089
DCF	Diclofenac	NSAID	<LOD	<LOD	-	
5H-DCF	5-hydroxy diclofenac	NSAID	<LOD	<LOD	-	
FLU	Fluoxetine	Antidepressant	7.83	<LOD	97	
IBP	Ibuprofen	NSAID	<LOD	<LOD	-	
LOS	Losartan	High blood pressure (hypertension)	6.54	13.73	-110	78
DMPA	Medroxy progesterone 17-acetate	Hormonal therapy	<LOD	<LOD	-	
MET	Metoprolol	Beta-blocker	465.80	388.38	17	8.6
DEET	N,N-diethyl-meta-toluamide	Insect repellent products	33.52	48.22	-44	24.68
NTP	Nortriptyline	Antidepressant	4.45	0.42	91	0.18505
PRE	Prednisolone	Corticosteroid	<LOD	<LOD	-	
RN	Ranitidine	Decrease stomach acid production	2.24	<LOD	95	
SMV	Simvastatin	HMG-CoA reductase inhibitors (statins)	19.49	<LOD	96	
SDX	Sulfadoxine	Ultra-long-lasting sulfonamide	<LOD	<LOD	-	
SMZ	Sulfametaxazole	Antibiotic	101.09	0.30	100	0.6
TMP	Trimetoprim	Antibiotic	7.93	5.47	31	120
TCPP	Tris (1-chloro-2-propyl) phosphate	Flame retardant and plasticizer	182.58	471.44	-158	260
WAF	Warfarin	Anticoagulant (blood thinner)	<LOD	<LOD	-	

Model of the wastewater discharged plume

- Based on Dose related Risk and Effect Assessment Model (DREAM), a numerical model for the release of complex mixtures of chemicals

- Plume prediction inputs:
  - Ocean currents
  - Discharge rates
  - Physical, chemical

  and toxicological properties of selected PPCPs



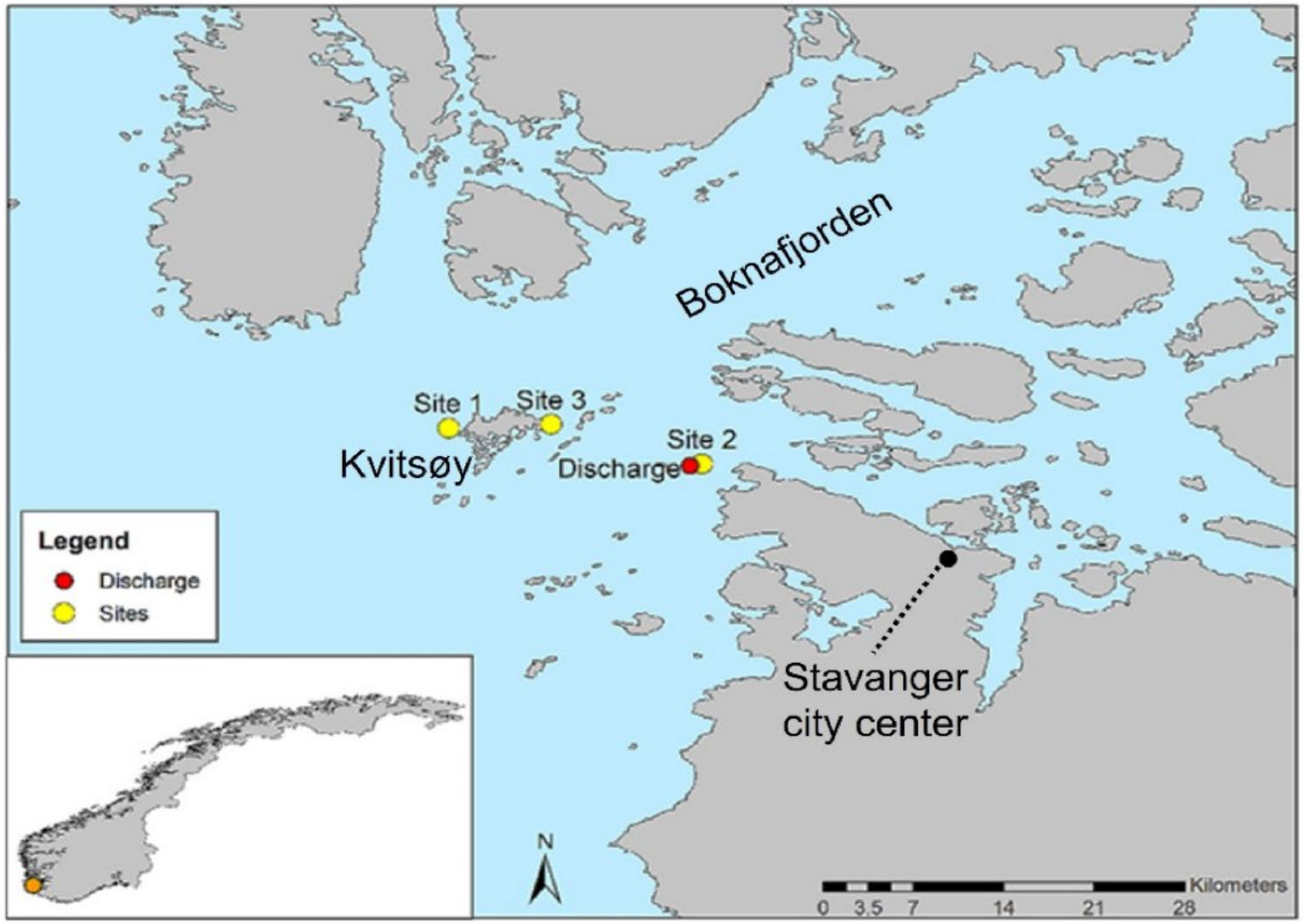
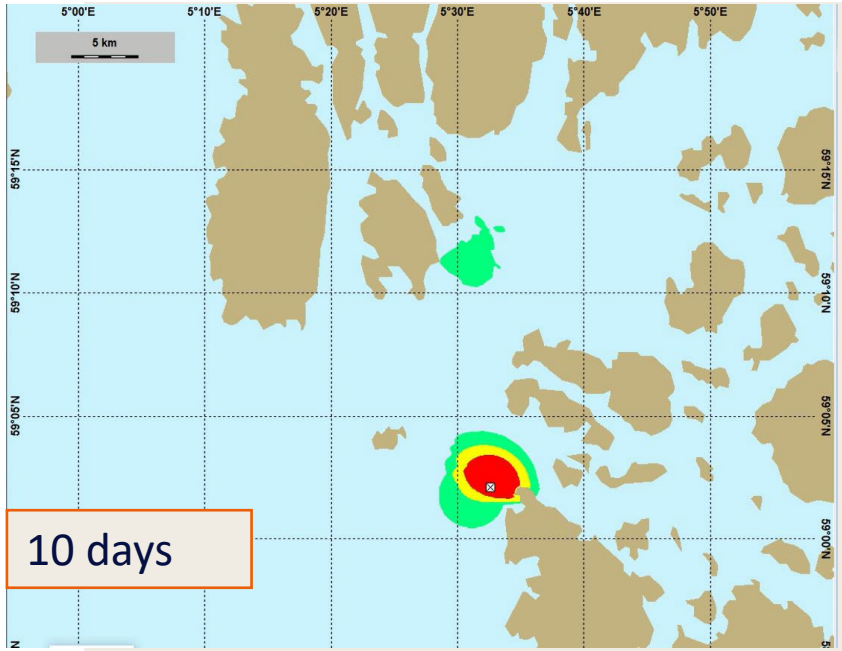
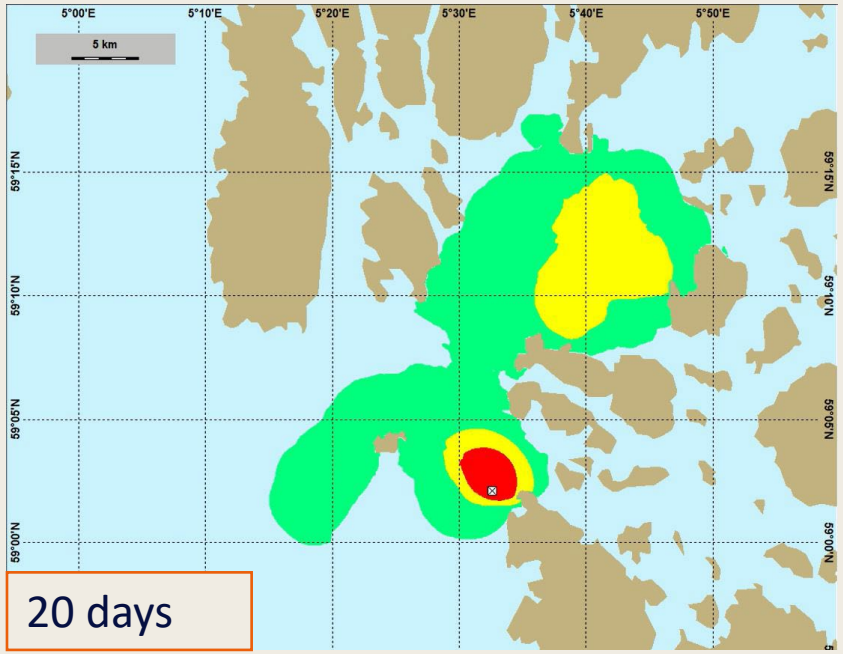
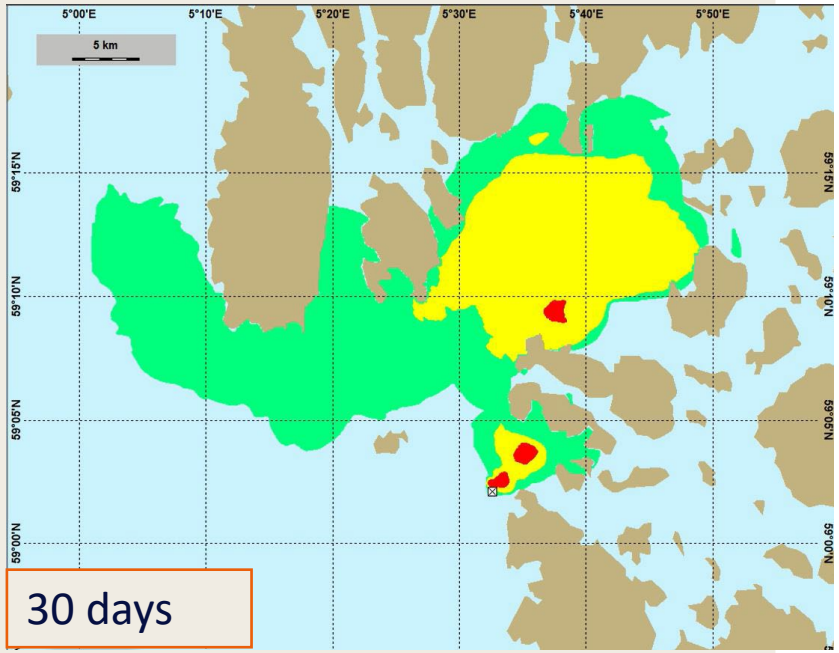


Fig. 1. Juvenile Atlantic cod (*Gadus morhua*) caging sites. Site 1 = reference, site 2 = wastewater treatment plant (WWTP) discharge location, site 3 = outside of WWTP plume. The red dot represents the exact location of the WWTP discharge point, 100 m south of site 2.

Distribution of PPCPs in the marine environment based on the model distribution







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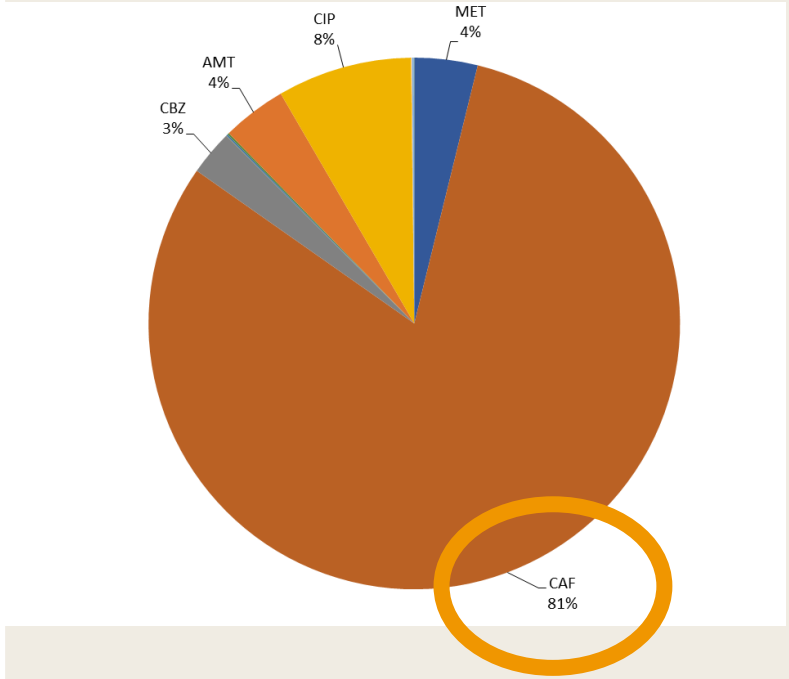
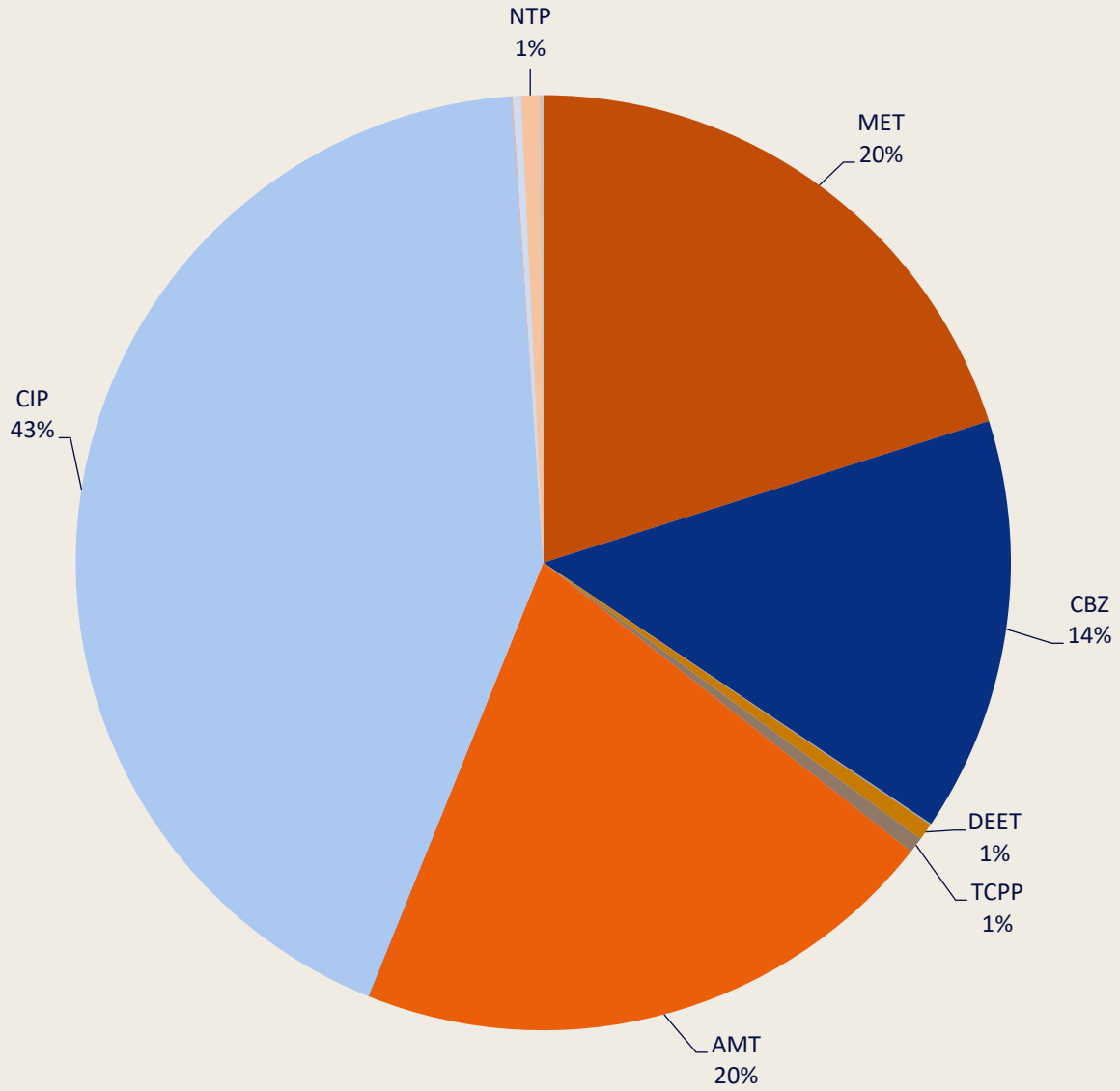
HQ<1….Relative contribution of PPCPs to the HQ





Ciprofloxacin 43%
Metoprolol 20%
Amitriptyline 20%
Carbamazepine 14%

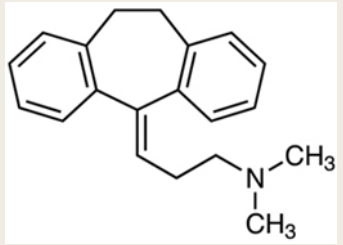
Amitriptyline

Sediment samples from the WWTP area

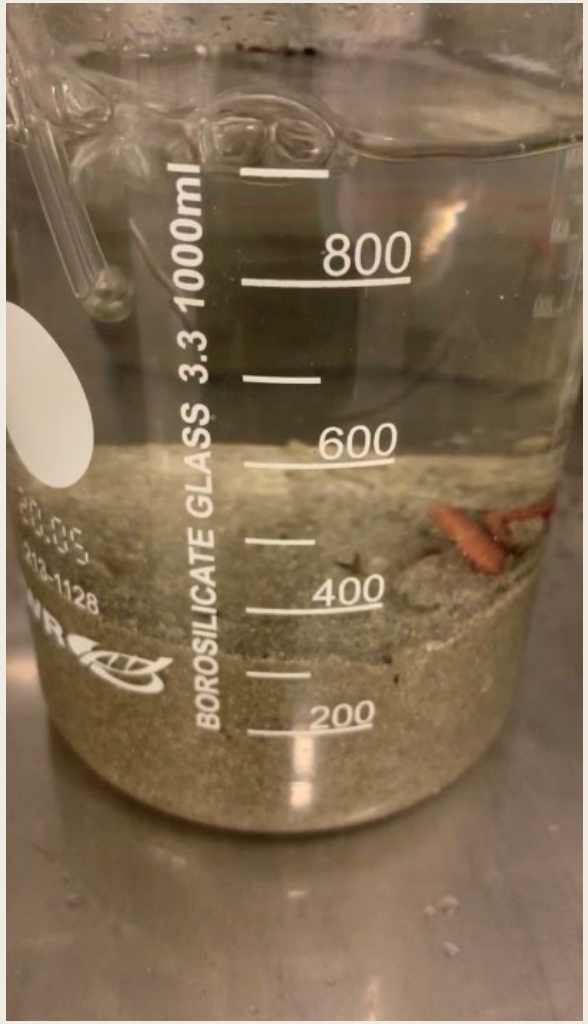
		Mean (ng/g)		
		Ref. 1	Ref. 2	WWTP
Non-Steroidal Anti-Inflammatory Drugs	Ketoprofen	n.d.	2	n.d.
Steroids	Methylprednisolone	13	n.d.	n.d.
Tricyclic Antidepressants	Amitriptyline	n.d.	n.d.	12

Amitriptyline is a **tricyclic antidepressant**.
It inhibits the re-uptake of norepinephrine and serotonin, thereby increasing their synaptic concentration.

The most prescribed antidepressant in Norway.



28 Day Chronic Sediment Exposures with a polychaetes (*Nereis virens*)



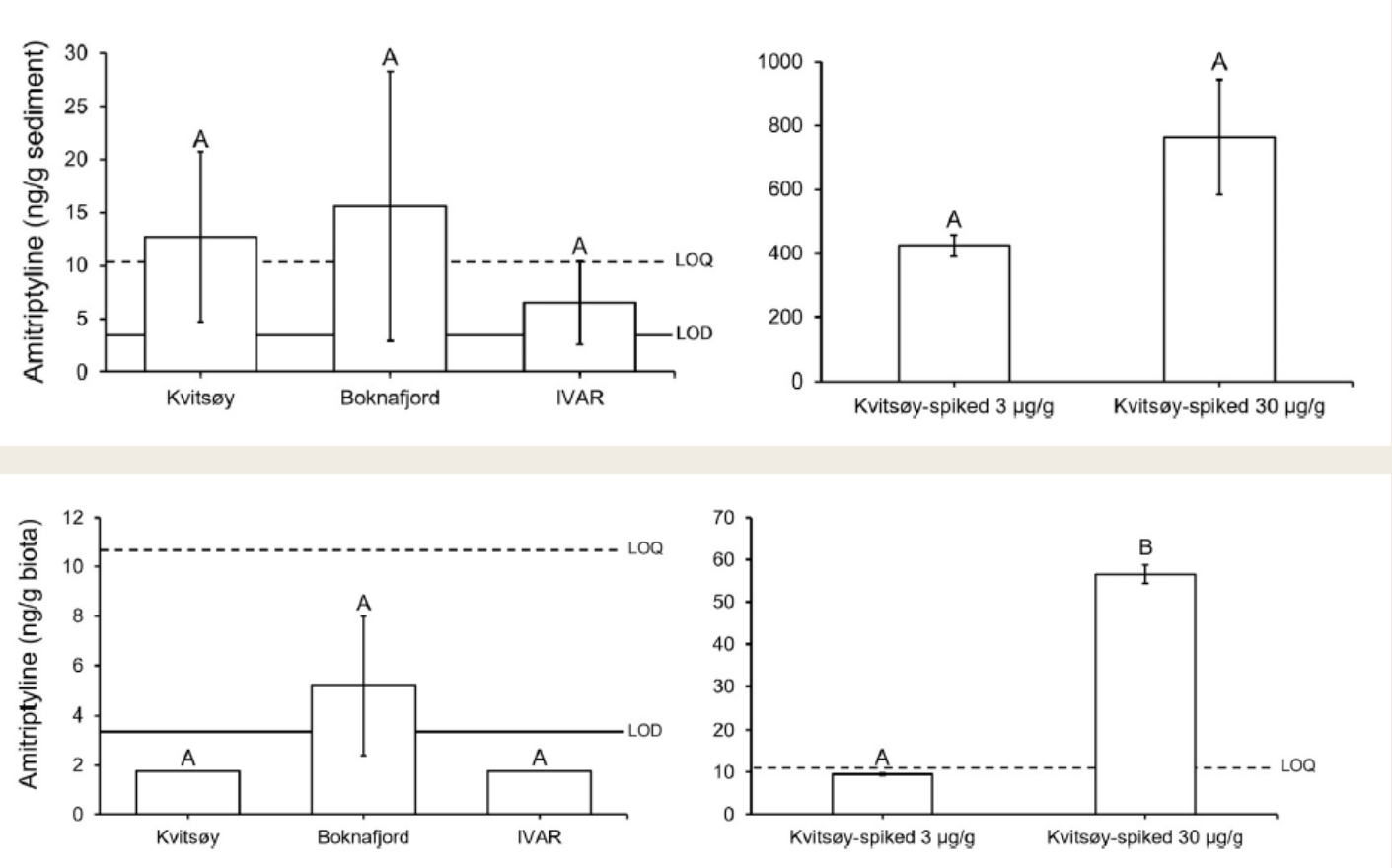
3 field sediments
1 ref sediment spiked (2 concentrations)
1 ref spiked with solvent (carrier)

Chemical Analysis of Amitriptyline in sediment, biota and water

LC-MS/MS analysis

Bioaccumulation potential of the tricyclic antidepressant amitriptyline in the marine polychaete.

Positive correlation between the concentration of amitriptyline in sediment samples and body burden concentrations in *N. virens.*



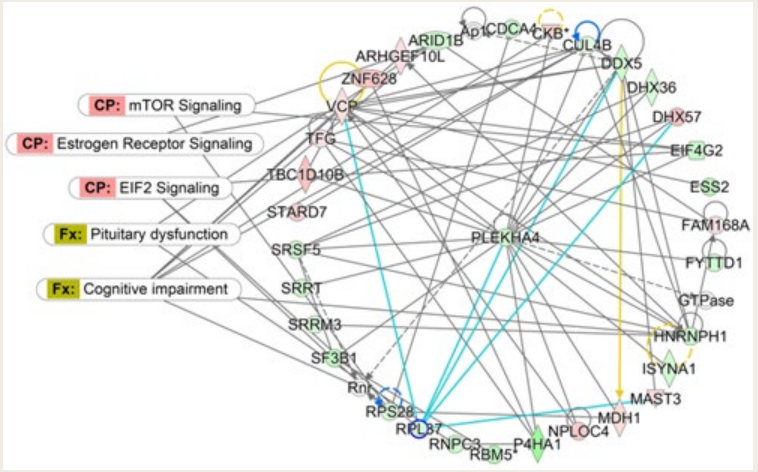
Sediment

Biota

Amitriptyline has the potential for trophic transfer following exposure to contaminated sediments.

(Magnuson et al. 2022)

Effect of Wastewater Treatment Plant Discharge on Juvenile Atlantic Cod (*Gadus morhua*) Brain Transcriptome



RNA Sequencing in brains - males and females → INGENUITY PATHWAY ANALYSIS → Canonical pathways
Disease and functions

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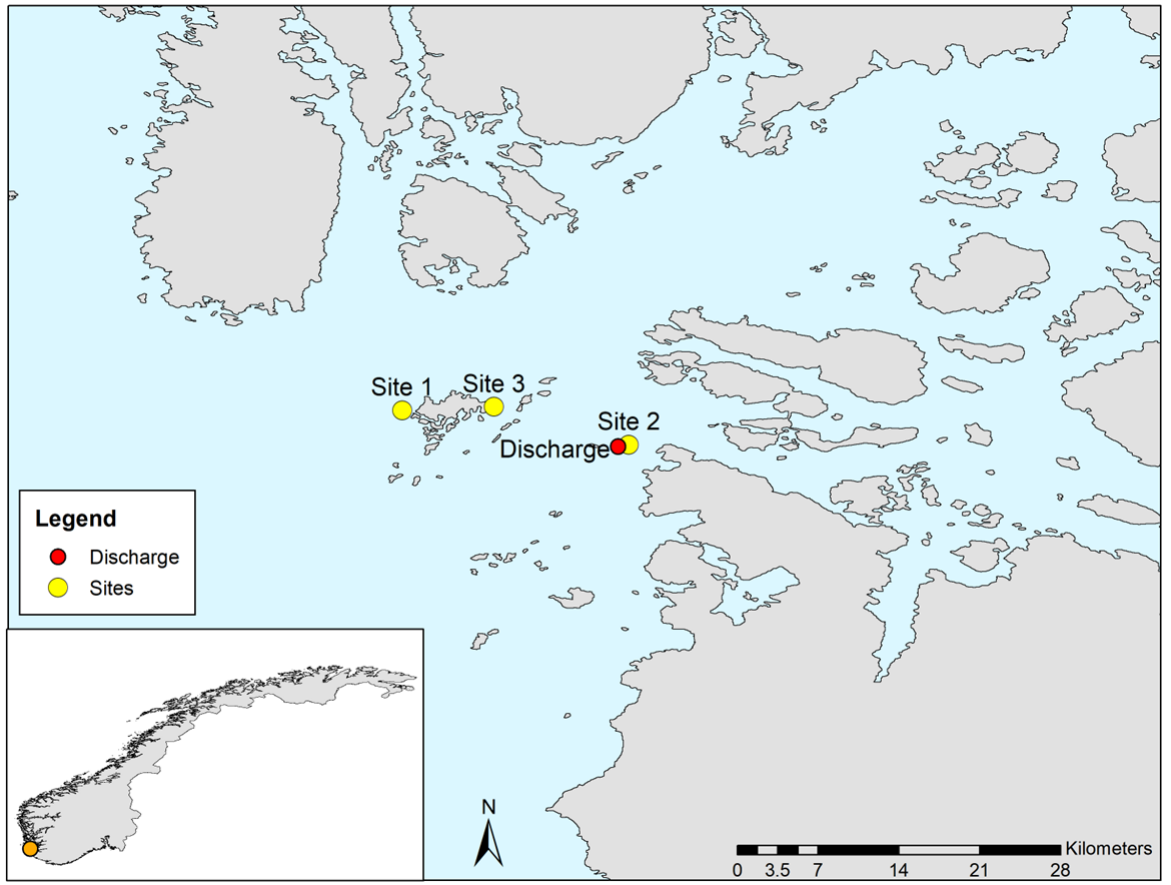
Experimental design

- Juvenile Atlantic cod (1 to 2 years old) caged for 4 weeks in Stavanger fjord

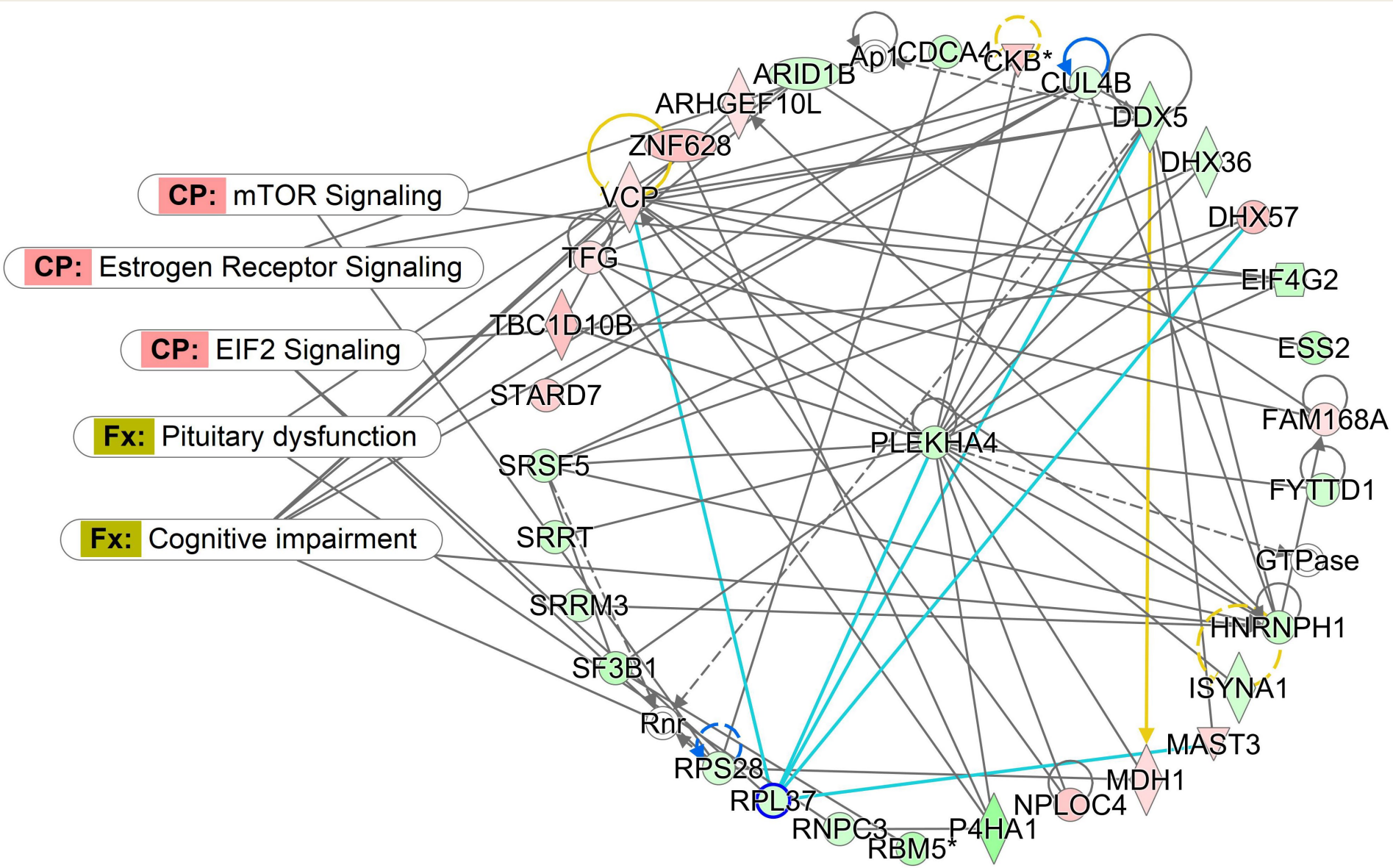
- Site 1 = Reference
  Site 2 = WWTP
  Site 3 = Salmon farm

- RNA Sequencing on brains- males and females

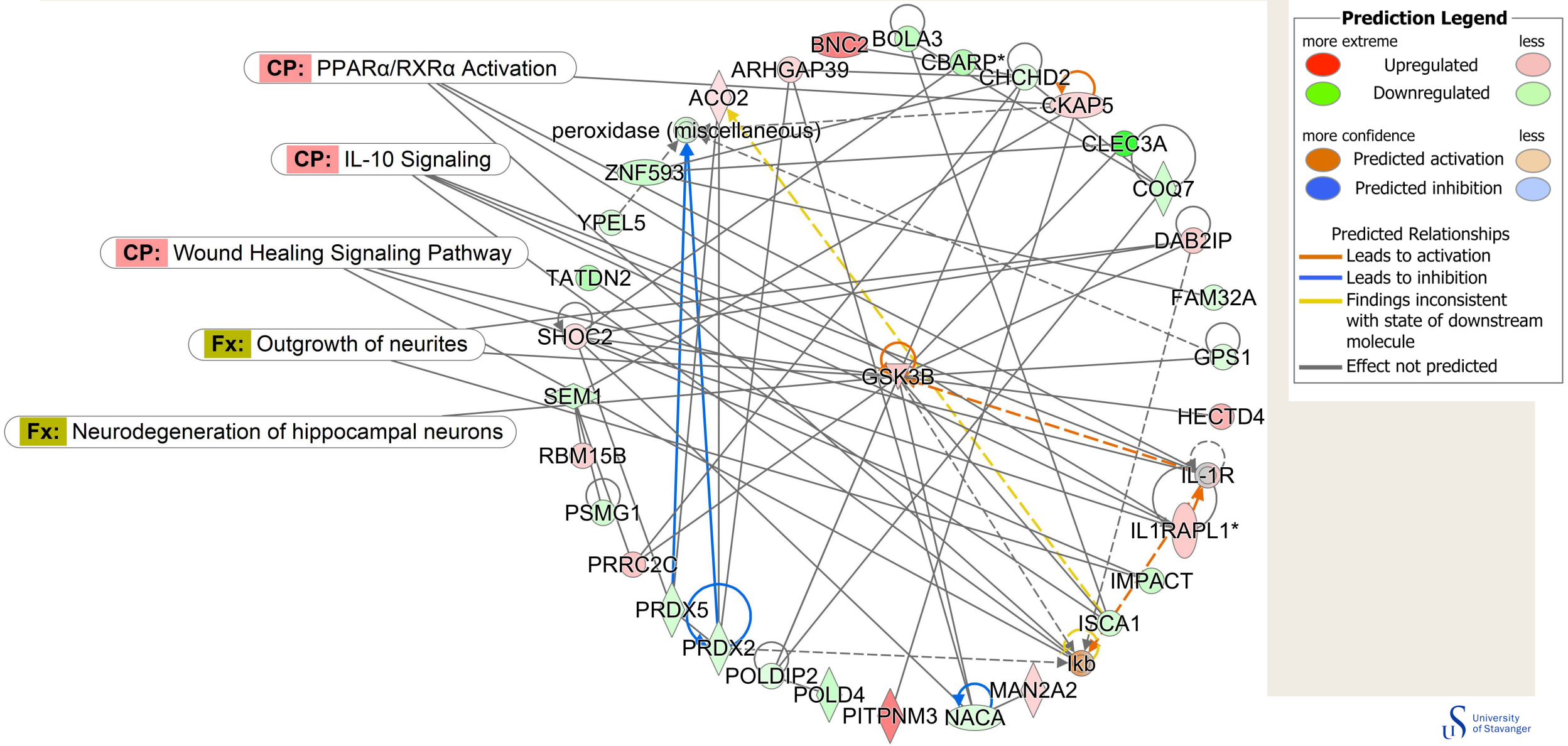
INGENUITY®
PATHWAY ANALYSIS



IPA prediction- Males at WWTP discharge point



IPA prediction- Females at WWTP discharge point



WP4 - SOCIAL BENEFIT-COST ANALYSIS

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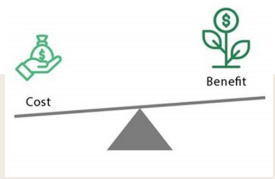
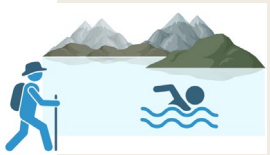


Giving an economical value to the PHARMASEA research work

The methodological process of estimating the economic value of:

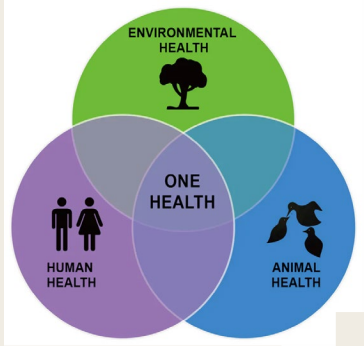
1) Environmental damages and emission of pharmaceuticals ("**hidden costs**"),
2) Protecting nature and improving environmental quality ("**hidden benefits**").



How much are «free» ocean recreation opportunities worth?

e.g. Photodegradable antibiotics

What are the benefits of more environmentally friendly (greener) pharmaceuticals?



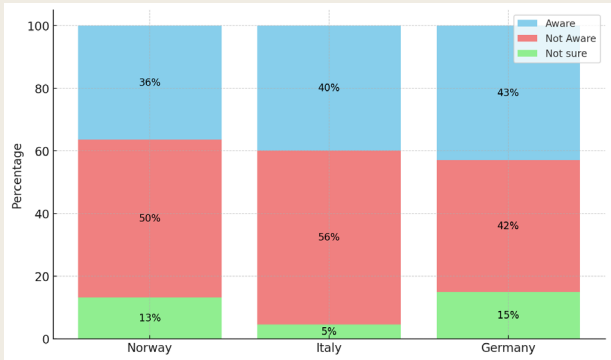
Do generational differences exist in environmental preferences for reducing pharmaceutical and personal care product emissions?

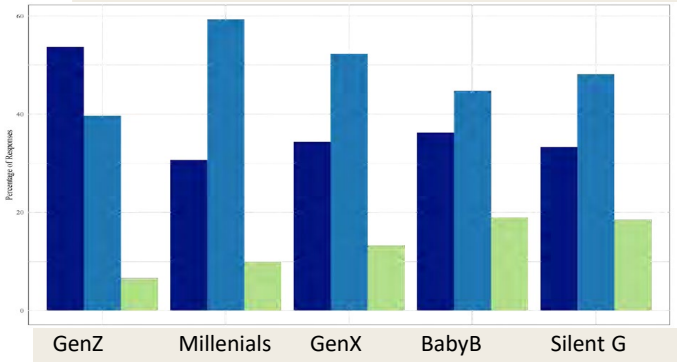
1 Are there differences in PPCP usage, disposal habits, and pollution awareness regarding the environmental impact of pharmaceutical waste across different generations?

2 What are the preferences of young and older individuals regarding the four proposed pharmaceutical waste disposal programs?

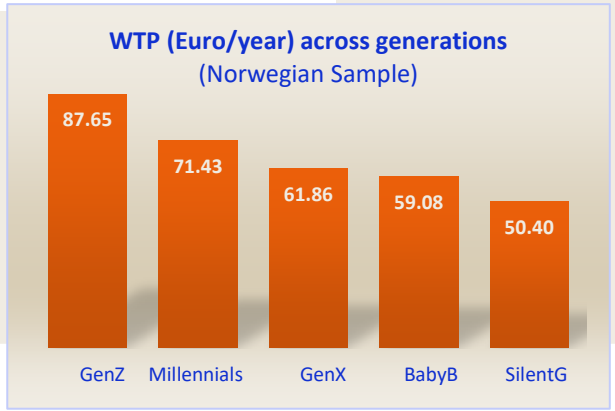
3 How does willingness to pay for a pharmaceutical disposal program vary across different generations?

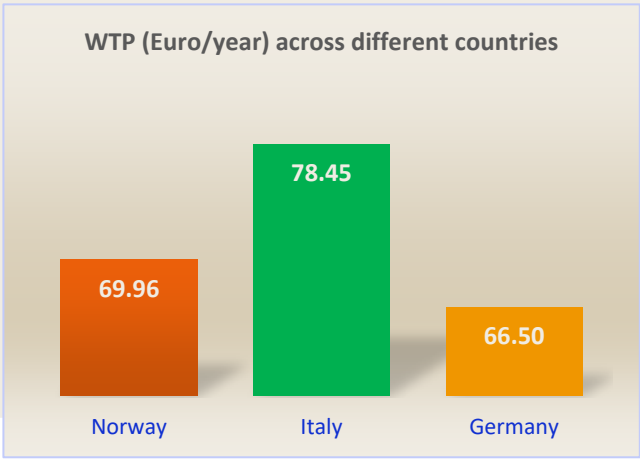
What about Italy and Germany?





Awareness of APIs as environmental challenges by generation in Norway





Conclusions

- Hazard quotient values of aqueous PPCPs <1
- Trophic transfer of some PPCPs possible
- Sublethal impacts noted in caged fish exposed to plume
- Age-dependent differences in awareness of PPCP issue and willing to pay (Norway)
  - Gen Z > Millenials> GenX>Babyboom>Silent G
- Geographical differences in awareness
  - Germany>Italy>Norway
- Geographical differences in willing to pay
  - Italy>> Norway>Germany

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