THE UNIVERSITY of York

Drugs down the drain: Impacts of medicines in the natural environment

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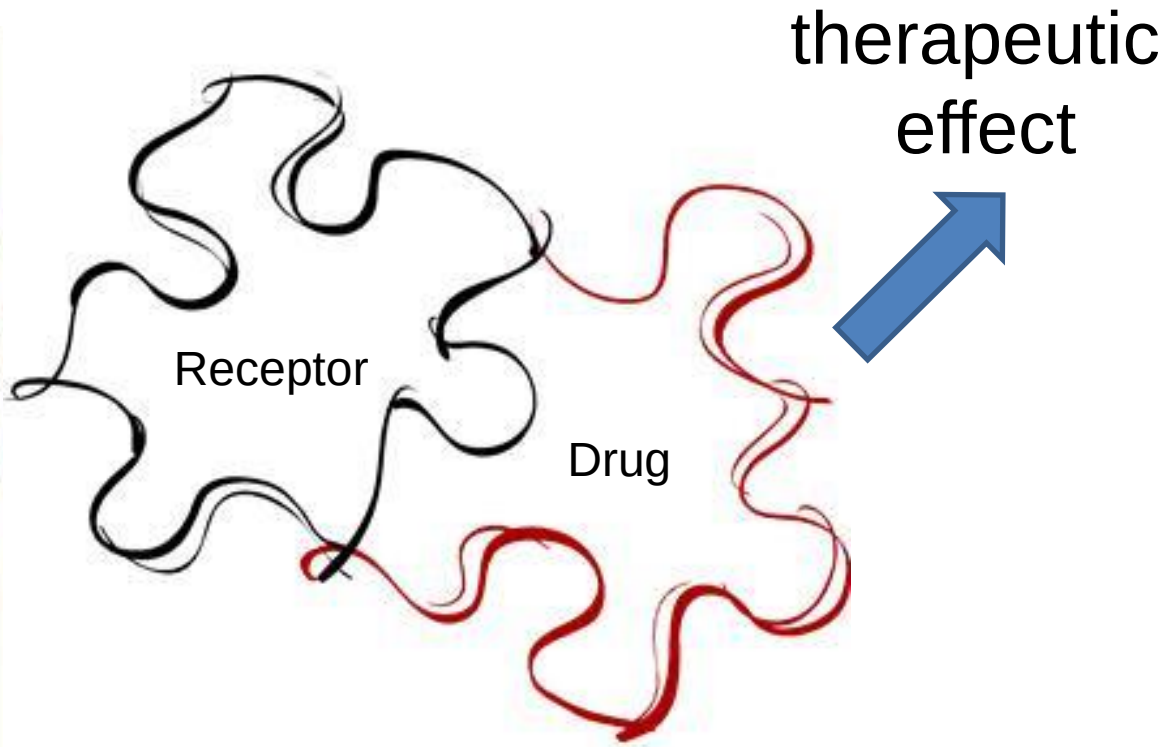
Environment Department


OcuFresh
Sleep Well
Aquaphor
RAHUA
M LAB.
PerioWash
Complete Oral Care

Drug receptors



Many receptors also occur in organisms in the natural environment

Effects on behaviour

Rebecca Klaper, Great Lakes Water Institute

Fathead minnow -

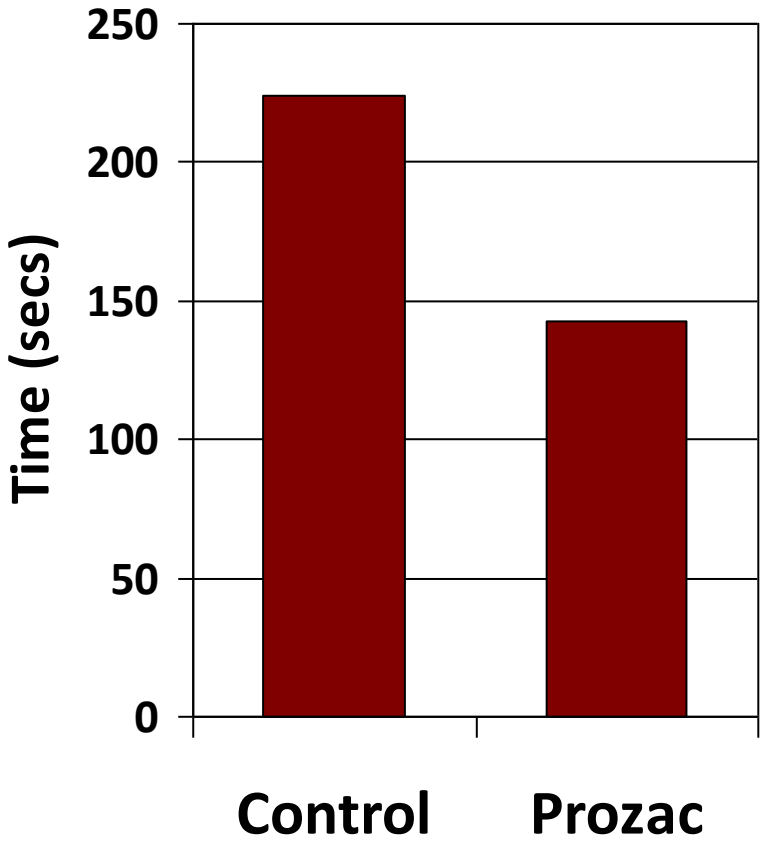
Lifecycle exposure

to Fluoxetine

100 ng/L

Behavioural change – males sitting under tiles, not pursuing females. Time spent on breeding behaviours was very low.

Effects of Prozac on woodlice



Effects on wildlife

Fluoxetine at environmentally relevant concentrations can significantly alter behaviour and physiology in starlings

Bean et al., 2014. Phils Trans Royal Soc B

‘Nine species of vultures in the wild numbered 40 million birds in the early 1980s. Today, only about 60,000 birds are left’

(Vibhu Prakash, Bombay Natural History Society)

Presentation today

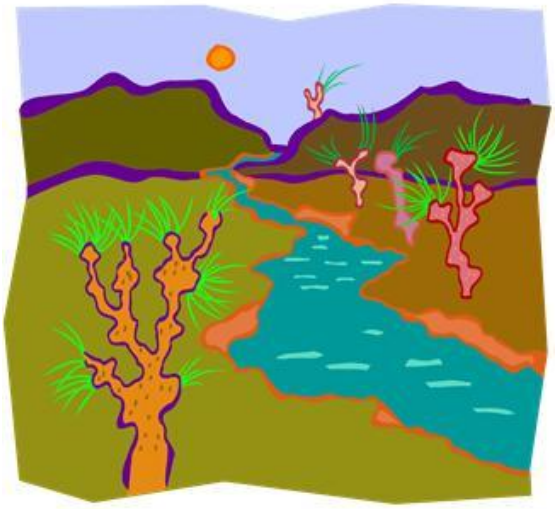
- Focus on aquatic systems in the UK
- What is the level of exposure at the landscape level?
- Could there be impacts?
- Could we manage these impacts?

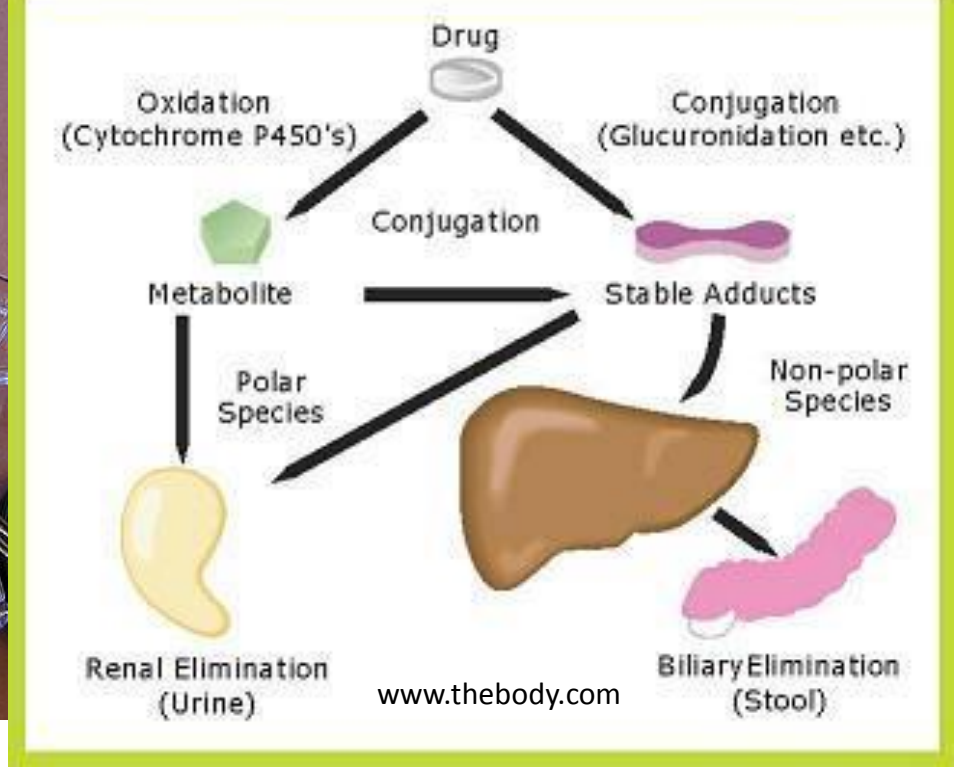
Typical approach to exposure modelling

Usage: mg person^{-1} d^{-1}
Metabolism: fraction excreted
Population size: persons

Removal: fraction removed
Wastewater flow: m^3 d^{-1}

River flow: m^3 d^{-1}
In-river dissipation rates: d^{-1}





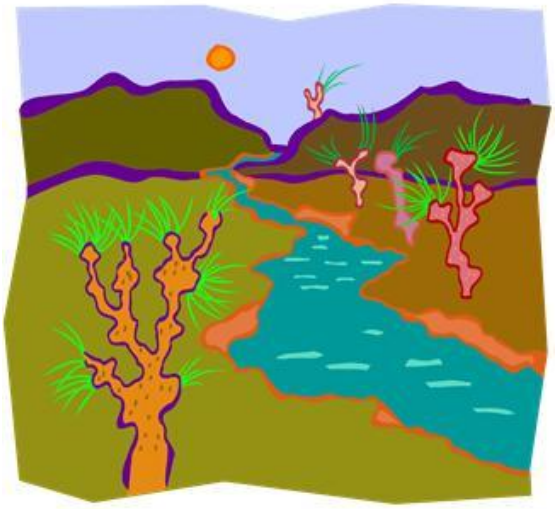
- Disposal: 3-65% of drugs not used
- Metabolism: differences depending on age, sex, race, health status (cyclophosphamide 2-25%)
- Wastewater treatment: differences in removal depending on technology and environmental conditions (diclofenac -143 to 80% removal)
- Variability in in-stream dissipation

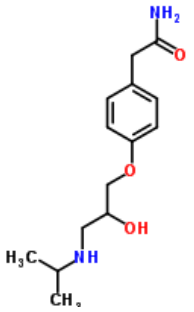
An alternative: inverse modelling

Usage

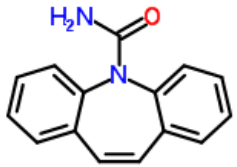
Overall removal between point of use and point of monitoring

Monitoring data

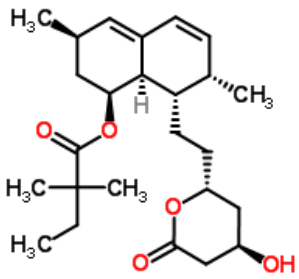




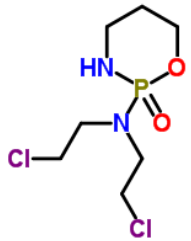
atenolol



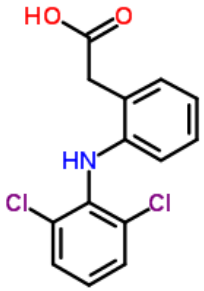
carbamazepine



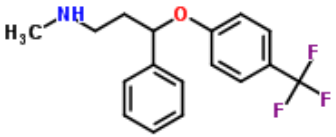
simvastatin



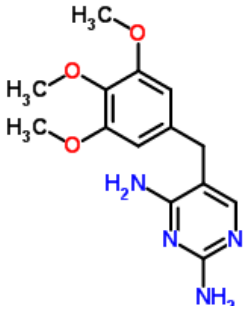
cyclophosphamide



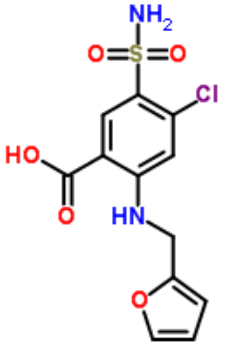
diclofenac



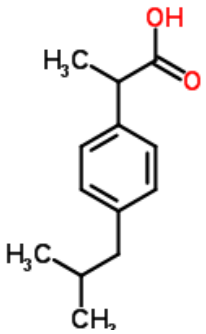
fluoxetine



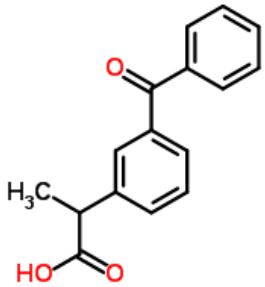
trimethoprim



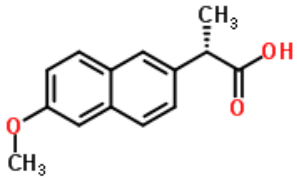
furosemide



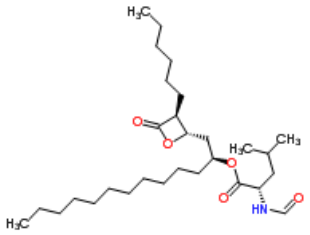
ibuprofen



ketoprofen

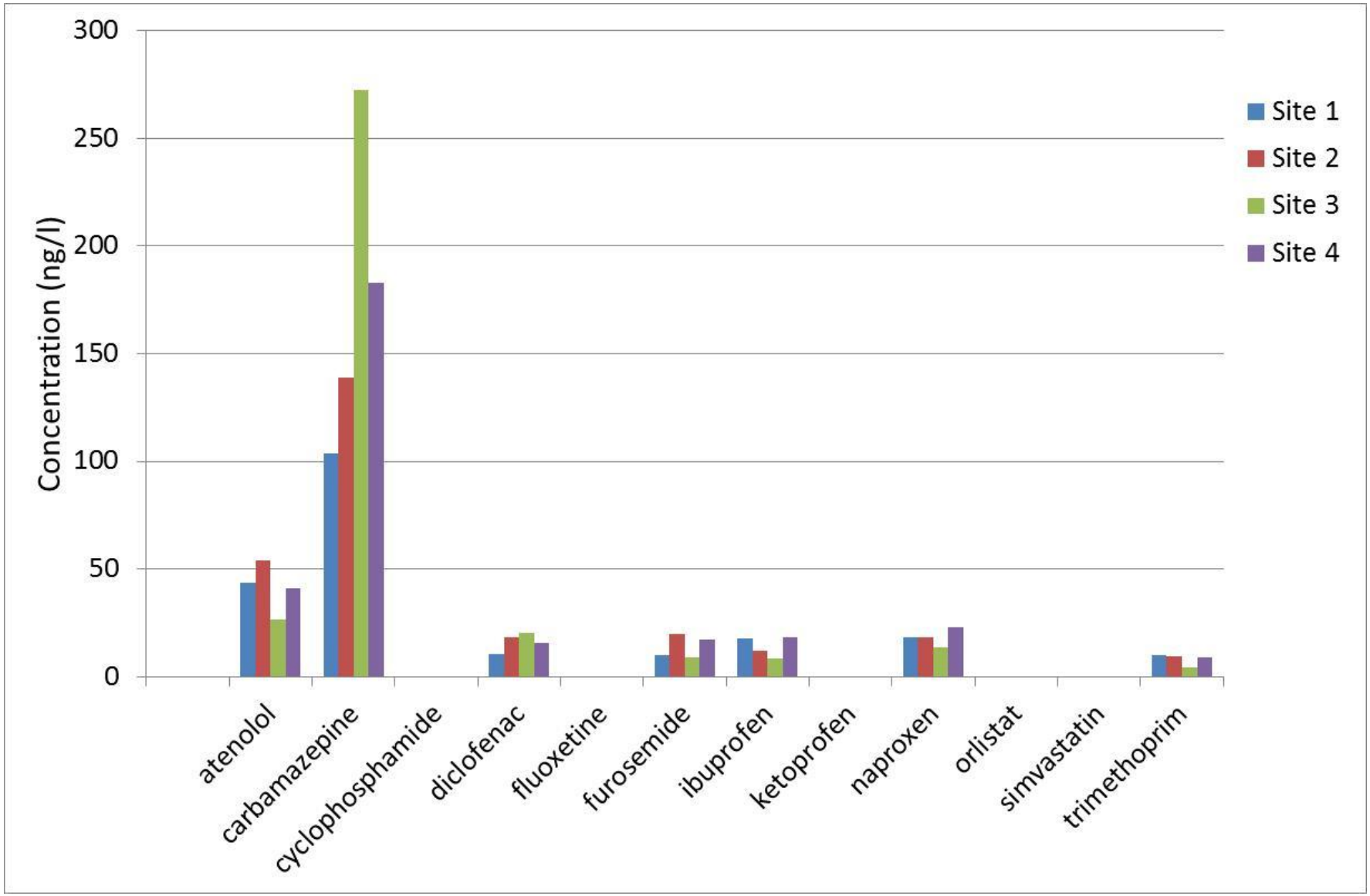


naproxen

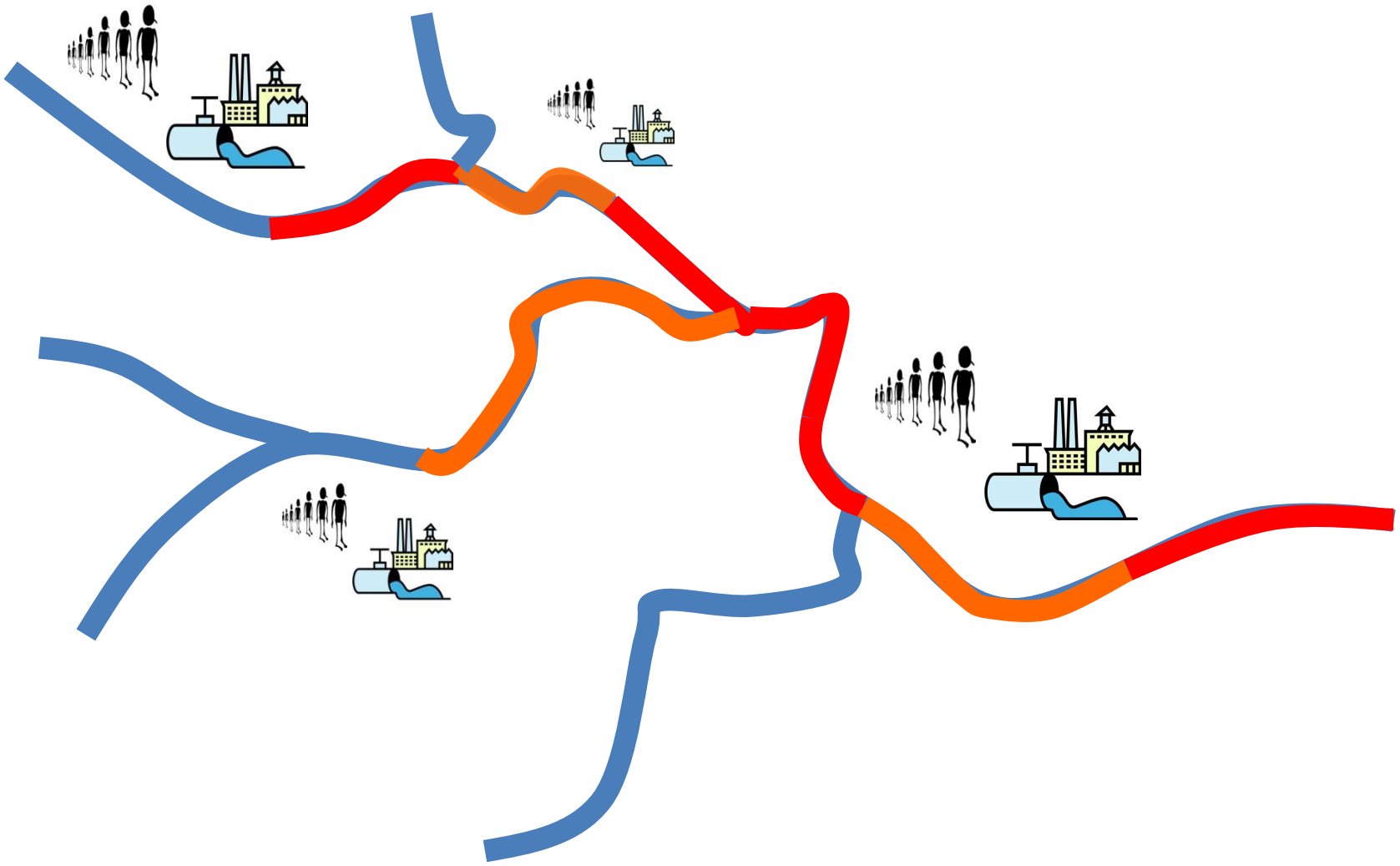


orlistat

Occurrence in UK rivers



Low Flows 2000 WQX Model



Applied to monitored pharmaceuticals using both the forward and inverse modelling approaches

Forward vs inverse-modelled removal rates

Compound	Inverse removal (%)	Forward removal (%)
Atenolol	93.92	4.0 – 97.9
Carbamazepine	90.63	69.0 – 89.1
Cyclophosphamide	> 95.36	—
Diclofenac	98.24	74.0 – 95.2
Fluoxetine	> 98.97	82.6 – 86.6
Furosemide	**98.18**	**10 – 77.5**
Ibuprofen	99.86	77.4 – 99.97
Ketoprofen	> 99.31	—
Naproxen	99.18	97.1 - 99.6
Orlistat	> 98.11	—
Simvastatin	> 98.42	—
Trimethoprim	**97.85**	**30-70.2**

Validation of the approach

Predicted and measured concentrations for selected pharmaceuticals in UK rivers: Implications for risk assessment

*Jonathan P. Bound, Nikolaos Voulvoulis**

Determination of selected human pharmaceutical compounds in effluent and surface water samples by high-performance liquid chromatography–electrospray tandem mass spectrometry

Martin J. Hilton*, Kevin V. Thomas

Analysis of OSPAR priority pharmaceuticals using high-performance liquid chromatography-electrospray ionisation tandem mass spectrometry

Paul H. Roberts*, Philippe Bersuder

The occurrence of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs in surface water in South Wales, UK

Barbara Kasprzyk-Hordern[a,b,], Richard M. Dinsdale[b], Alan J. Guwy[b]*

The occurrence of selected pharmaceuticals in wastewater effluent and surface waters of the lower Tyne catchment

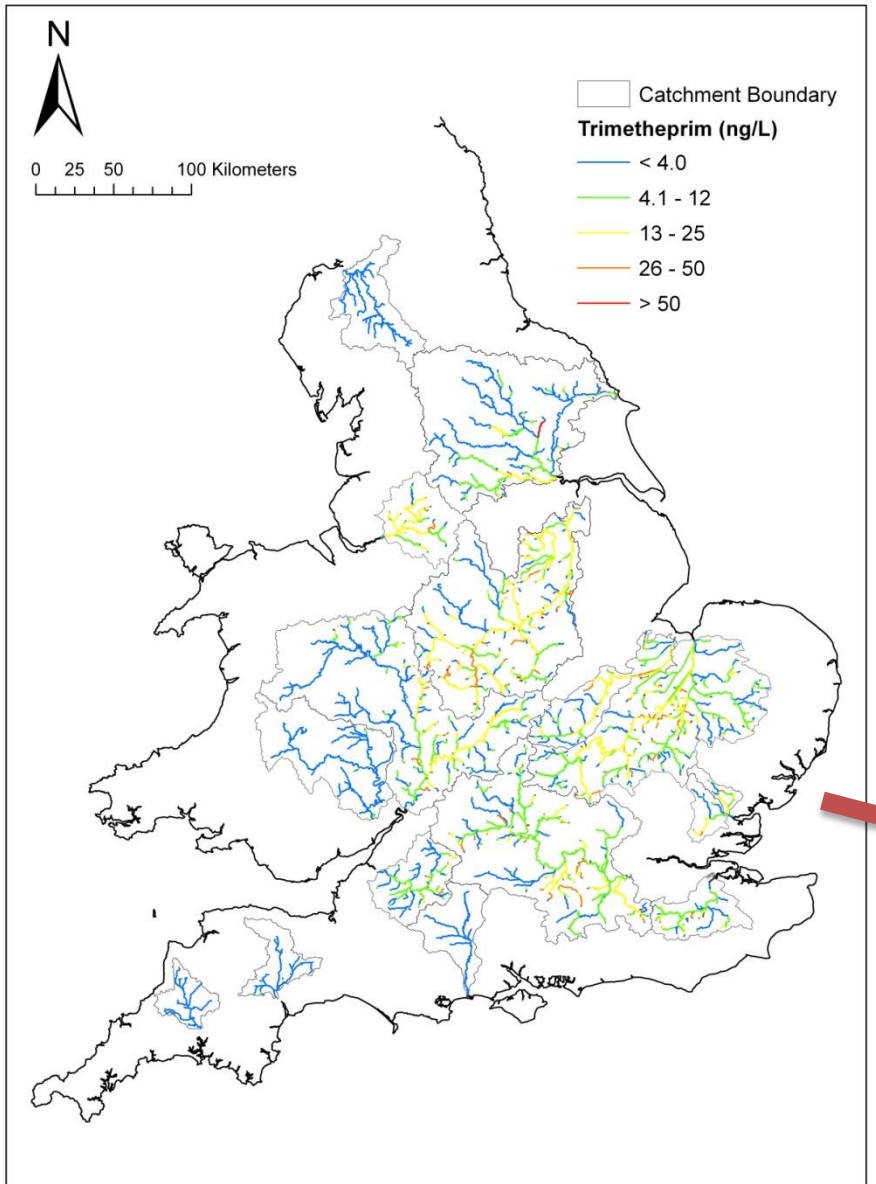
Paul H. Roberts*, Kevin V. Thomas

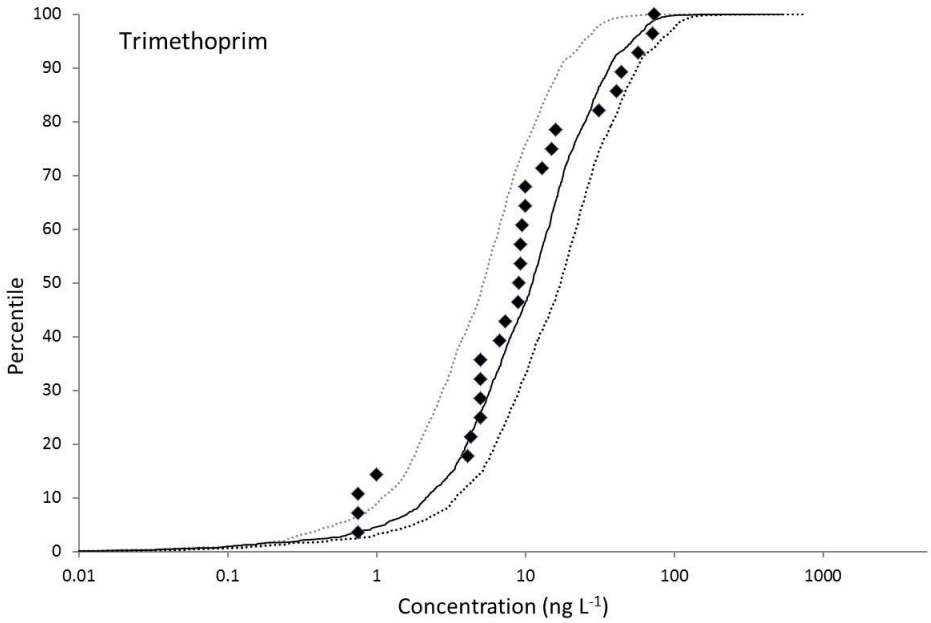
Simultaneous determination of various pharmaceutical compounds in water by solid-phase extraction–liquid chromatography–tandem mass spectrometry

Z.L. Zhang, J.L. Zhou*

Distributions of predicted concentrations developed for catchments that have been monitored and these were then compared to distributions of measured concentrations

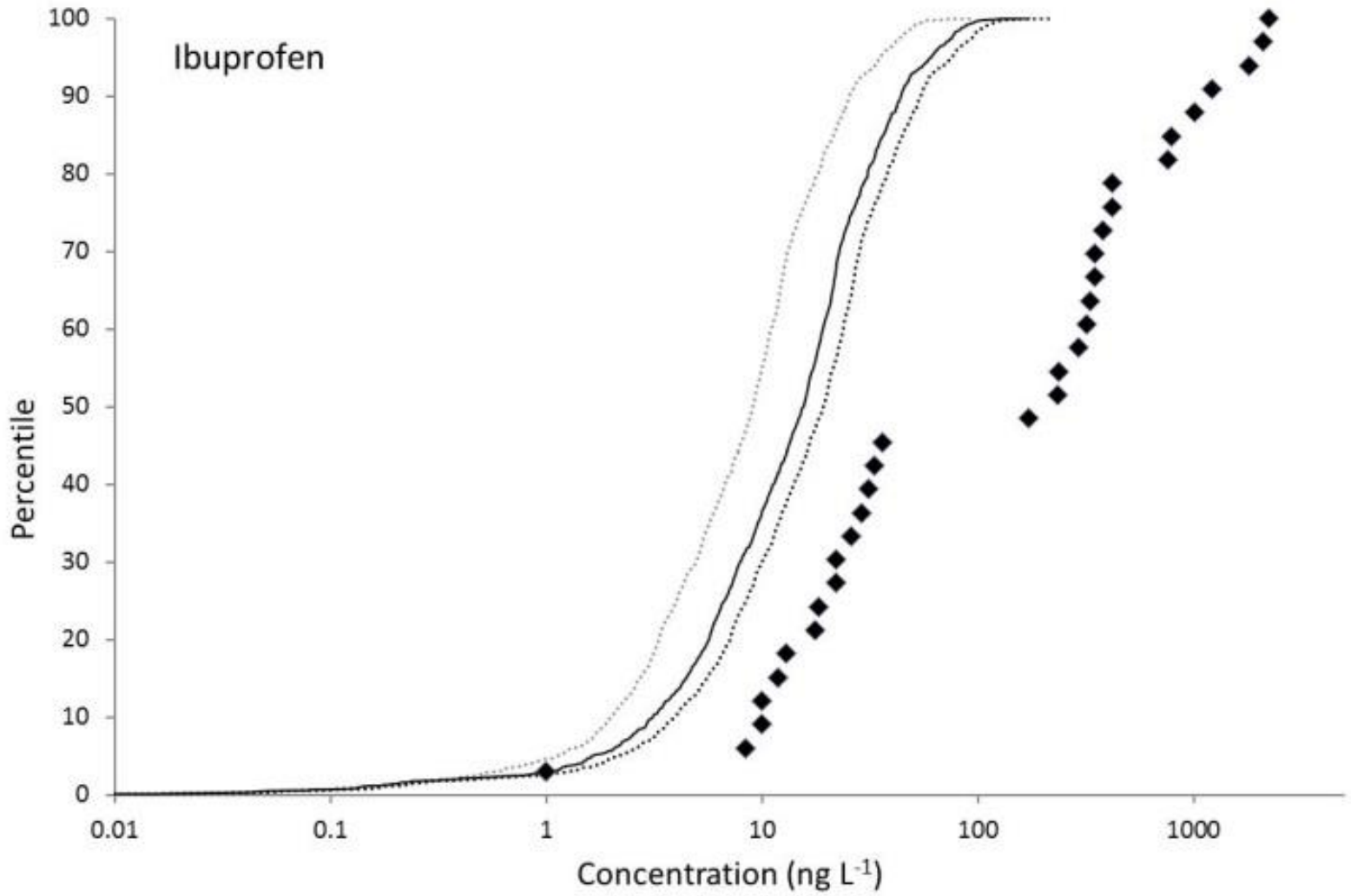
Concentrations of trimethoprim in monitored catchments



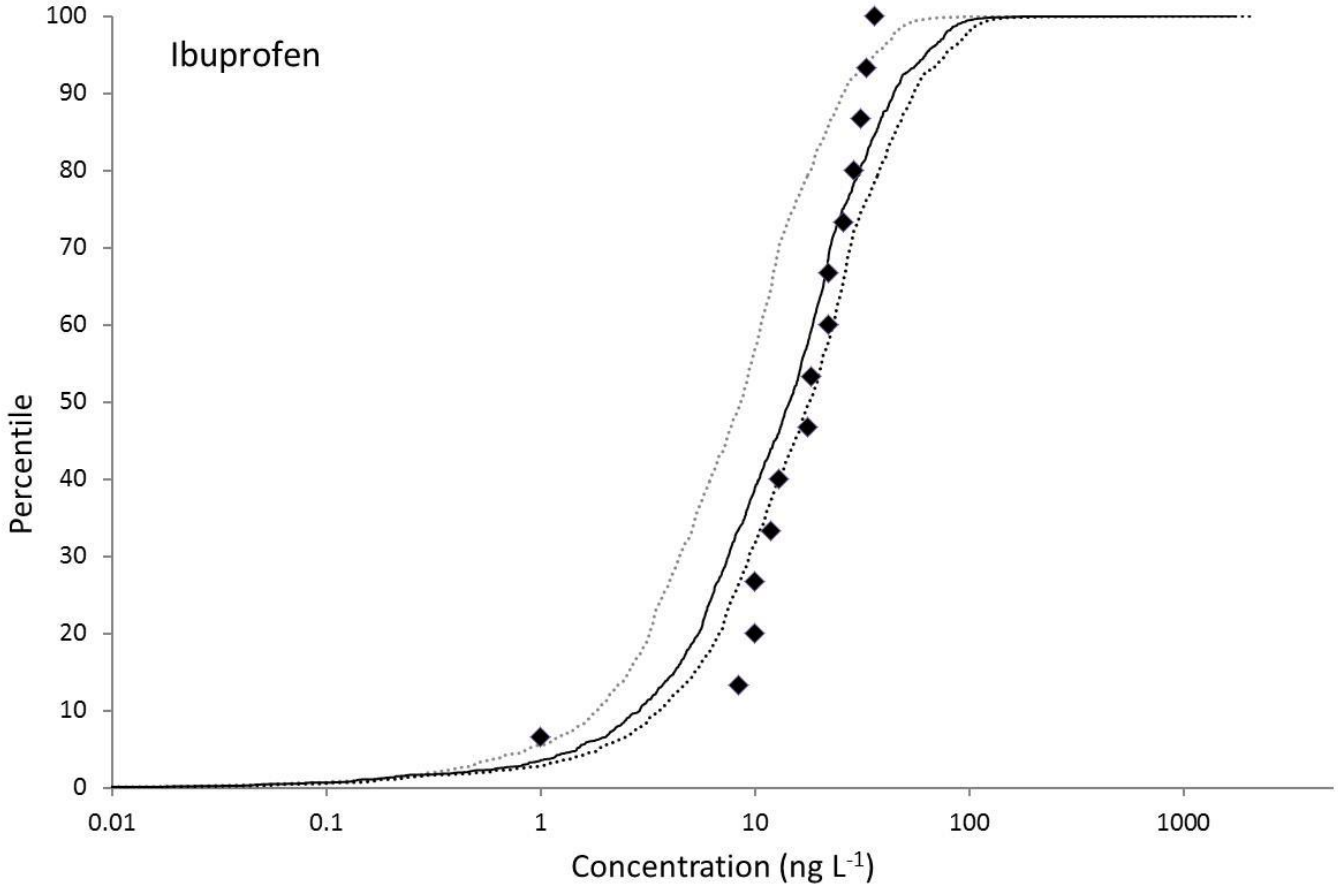


Predictions for each river reach obtained using mean, minimum and maximum removal rates obtained from the inverse modelling

Modelling vs monitoring



Ibuprofen – newer data



- Ibuprofen monitoring data dominated by studies done in early-mid 2000's
- Analytical technologies have advanced – removing e.g. matrix interferences
- Slight decrease in usage
- Tighter legislation – e.g. EU Freshwater Fish Directive, 2006

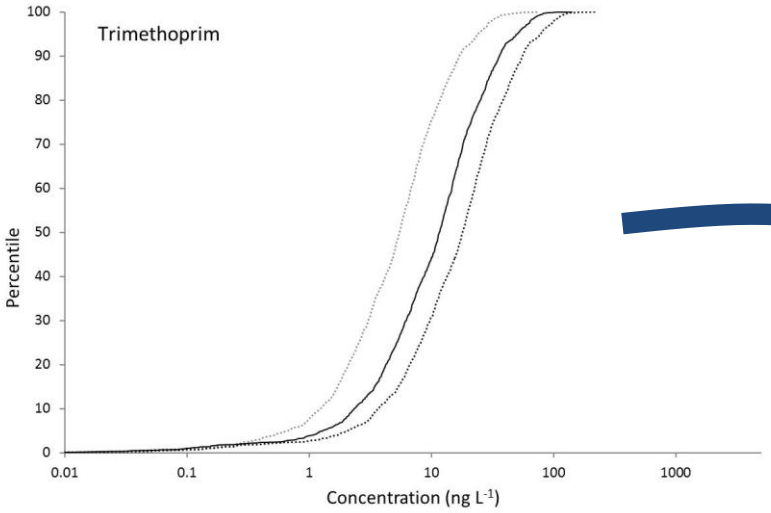
What are the effects?

- Modelling approach seems to work very well
- Review of literature and on-line databases done to pull out data on effects in aquatic systems
- Predicted no-effect concentrations derived from these data

Assessment of risks across the UK landscape

- 22 large catchments across England and Wales
- Serving a population of 21 M people
- Predictions obtained for 3117 river reaches
- Predictions compared to predicted no effect concentrations (and proposed quality standards) derived from available ecotoxicity data

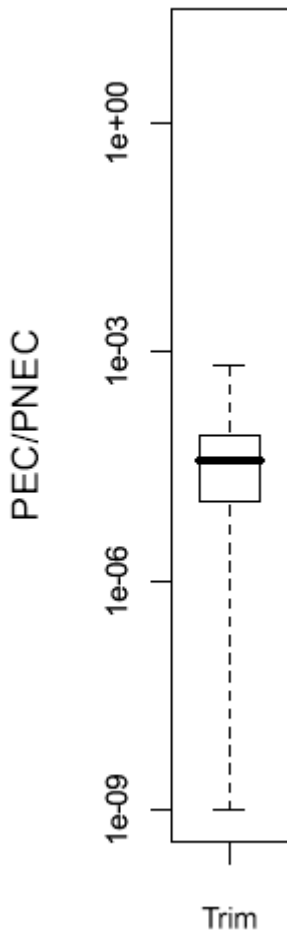
Risk characterisation



$$RCR = \frac{PEC}{PNEC}$$

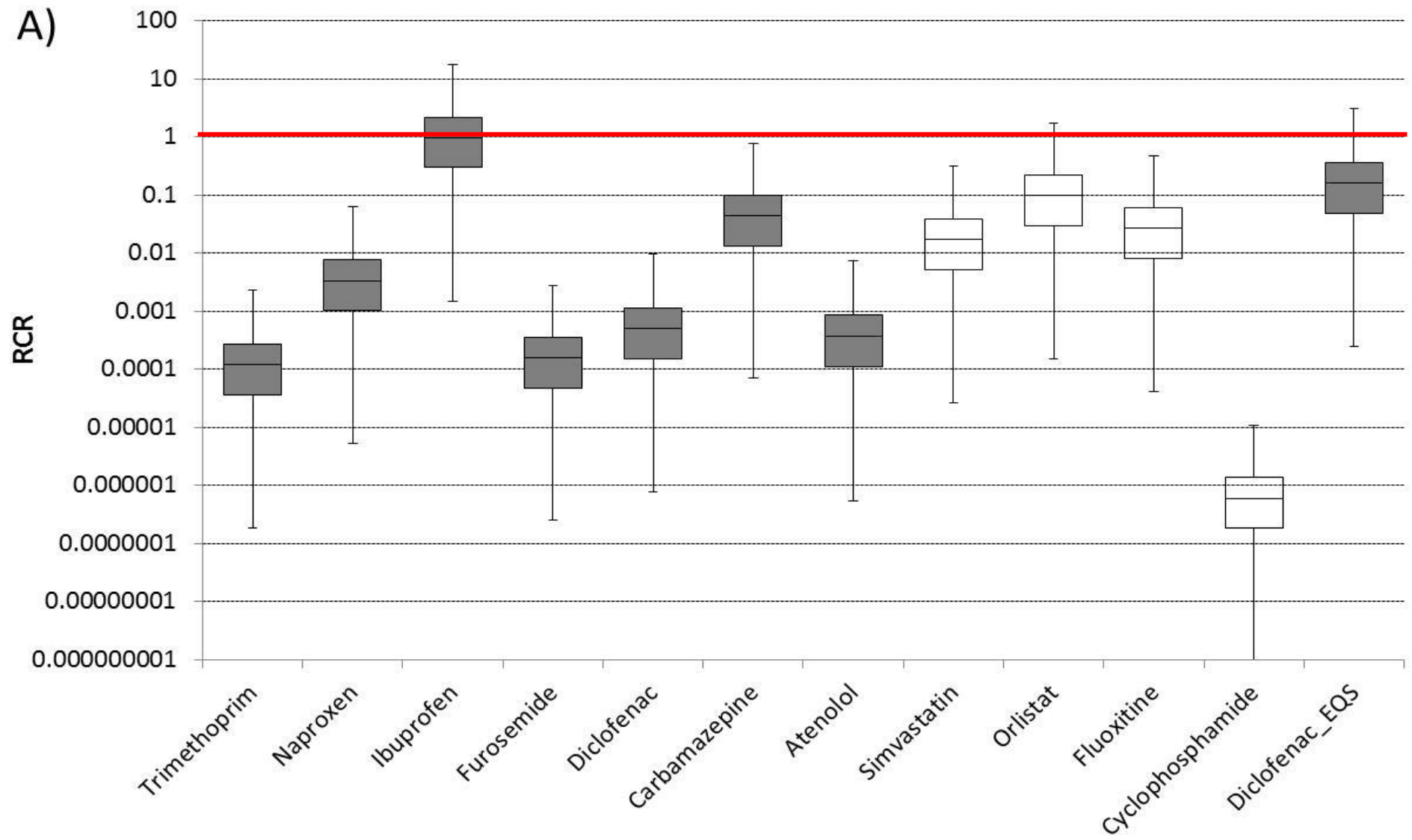
$$PNEC = \frac{ECx}{AF}$$

Or



WFD proposed EQS

Risk to UK Waters



Risk characterisation

- 45.5% of modelled river reaches (around 1500 reaches) have concentrations of ibuprofen of potential concern (fish hatching)
- 4.5% of modelled reaches (around 150 reaches) have concentrations of diclofenac of concern (histological effects)
- Are these effects occurring in reality?
- What can be done to control the risks?

Benign by design

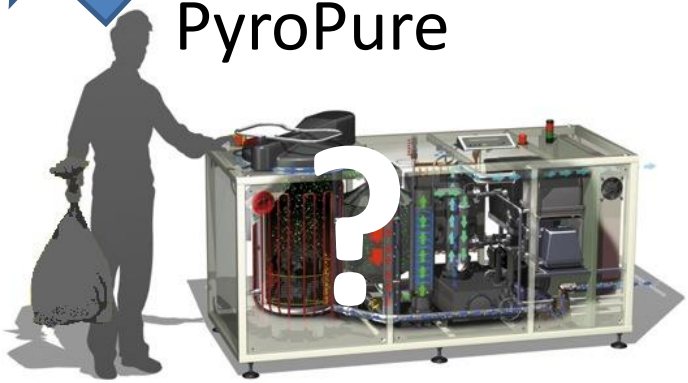
Upgrade sewage treatment plants

Reduced Pharmaceuticals in the environment

Stewardship schemes

www.ourlocal pharmacy.com

PyroPure



PyroPure

17 Pharmaceuticals selected

Decomposition Range 195-704°C

Non Steroidal Anti-Inflammatory Drugs

- Ketoprofen
- Ibuprofen
- Diclofenac
- Indomethacin

Analgesic

Ca-channel blocker: Verapamil

Beta-blocker: Atenolol

Anti-Parkinsons: Amantadine

Antidepressant: Fluoxetine

Anti-cancer: 5-fluorouracil

Hormones

- Estradiol
- Ethinyl-estradiol

Anti-gout:
Allopurinol

Antibiotics

- Chloramphenicol
- Sulfamethoxazole

Anti-diabetes:
Gliclazide

Anti-epilepsy: Carbamzepine

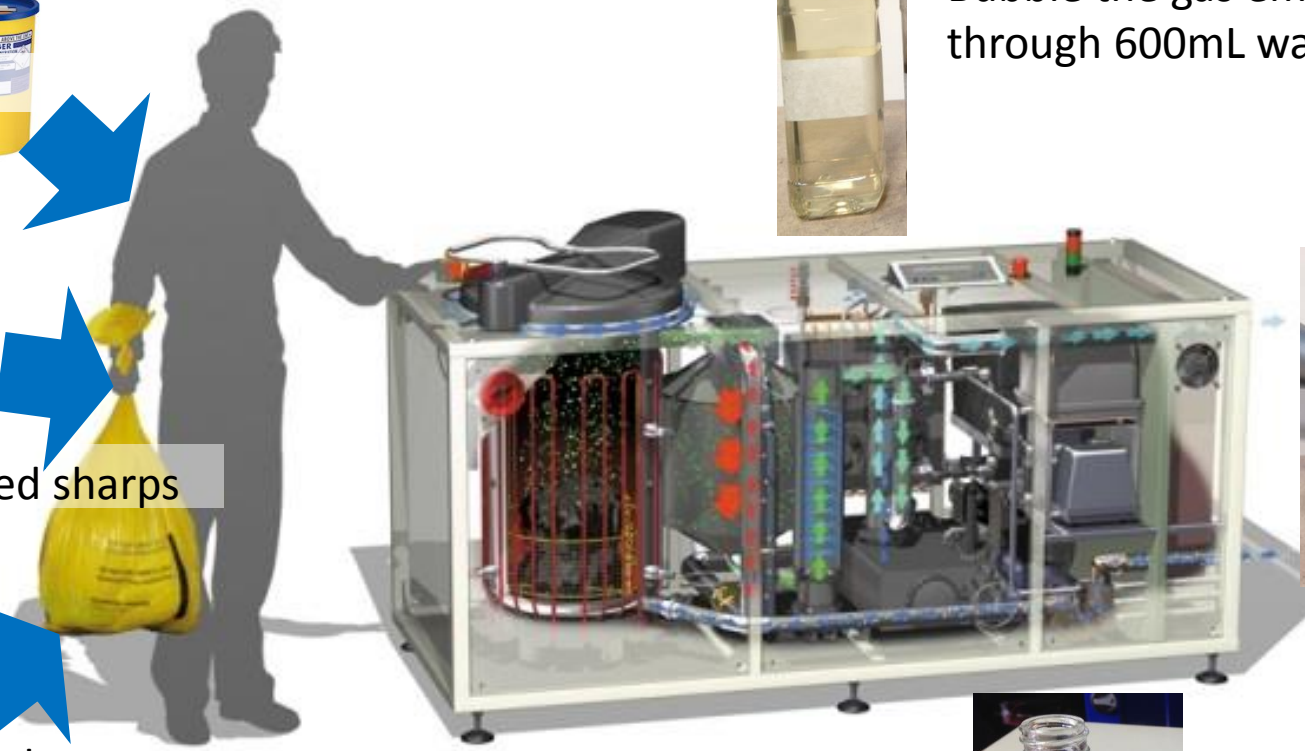
Experimental structure

3 Waste streams: For each 3 Pharmaceutical runs and 2 control runs

Take back medicines

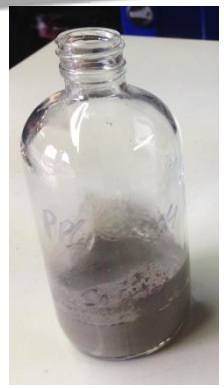
Contaminated sharps

Contaminated manufacturing waste



Bubble the gas emission through 600mL water

3 effluent samples per run



Collect all the solids (sludge)

Total of 15 runs: 5 for each waste stream

Main results

- Greater than 99% destruction of all pharmaceuticals achieved in all waste simulations
- No known degradation products seen

Summary

- Major concerns over pharmaceuticals in the environment
- Inverse modelling offers a number of advantages over traditional modelling approach
- Excellent agreement between model predictions and available monitoring data
- Approach appears to be effective at estimating exposure for different regions in a country the size of England.
- A significant proportion of river reaches in the UK may be at risk so some compounds require further scrutiny
- Results show the strength of integrating modelling with monitoring
- A range of management options available and there is a need for an integrated approach

Acknowledgements

Co-authors

- Sara Monteiro
- Richard Fussell
- Richard Williams
- Jurg Oliver Straub
- Virginie Keller
- Tom Bean
- Jane Thomas Oates
- Ed Bergstrom
- Amy Coulson
- Peter Bartl
- Kate Arnold

Technology Strategy Board
Driving Innovation

PyroPure