



Ecotoxicity Risks During an Influenza Pandemic

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“Dilution is the Solution to Pollution”

- Many drugs are minimally metabolised in the body.
- As a general rule, if a drug persists in the body it will likely persist in the environment.
- The problem is when a drug is used in sufficient quantity, such that its dilution in rivers is insufficient to lower its potential toxicity.



Dilution of Acutely Toxic Drugs

Do cytotoxic chemotherapy drugs discharged into rivers pose a risk to the environment and human health? An overview and UK case study

Andrew C. Johnson ^{a,*}, Monika D. Jürgens ^a, Richard J. Williams ^a, Klaus Kümmeler ^b, Andreas Kortenkamp ^c, John P. Sumpter ^d

Cytotoxics (Chemotherapy)



ELSEVIER

Available online at www.sciencedirect.com



Science of the Total Environment 373 (2007) 250–269

Science of the
Total Environment
An International Journal for Scientific Research
into the Environment and its Relationship with Humankind

www.elsevier.com/locate/scitotenv

Estrogen (Oral contraceptive)

An assessment of estrogenic organic contaminants in Canadian wastewaters

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PAPER

www.rsc.org/jem | Journal of Environmental Monitoring

Using environmental analytical data to estimate levels of community consumption of illicit drugs and abused pharmaceuticals†

Jonathan Bones, ^a Kevin V. Thomas ^b and Brett Paull ^{*a}

Received 23rd February 2007, Accepted 1st May 2007

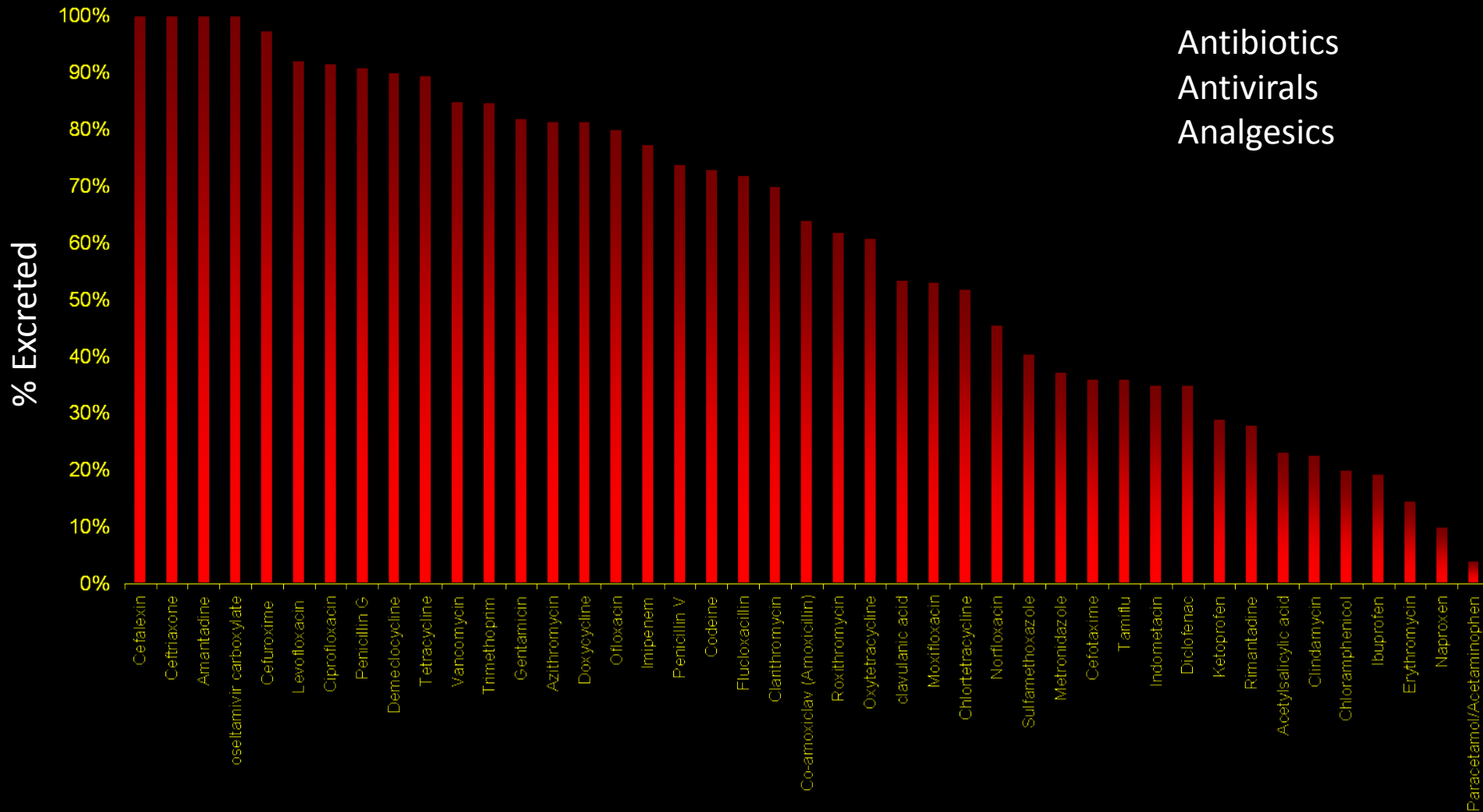
First published as an Advance Article on the web 17th May 2007

DOI: 10.1039/b702799k

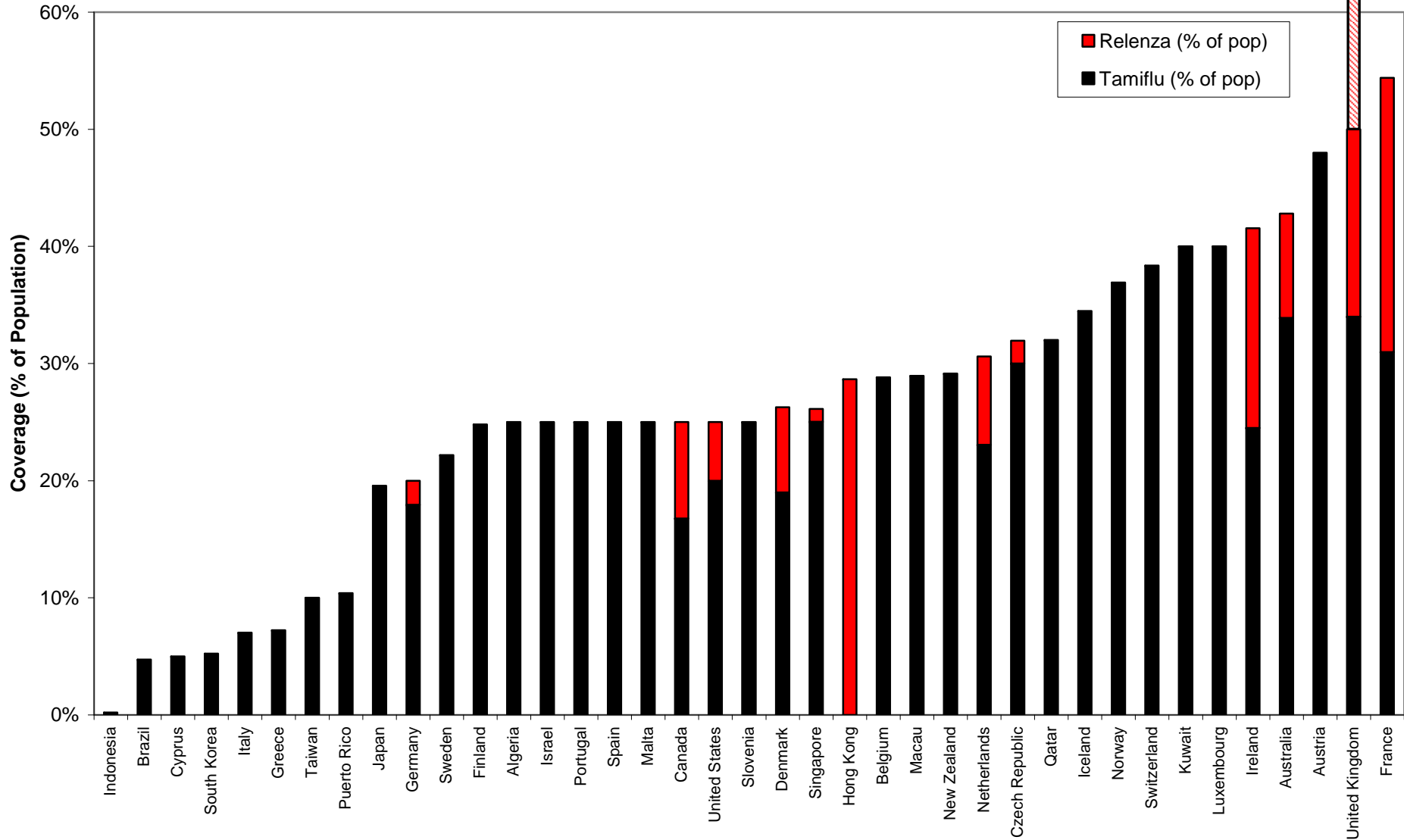
Cocaine, etc

Amount excreted as % of ingested

Antibiotics
Antivirals
Analgesics



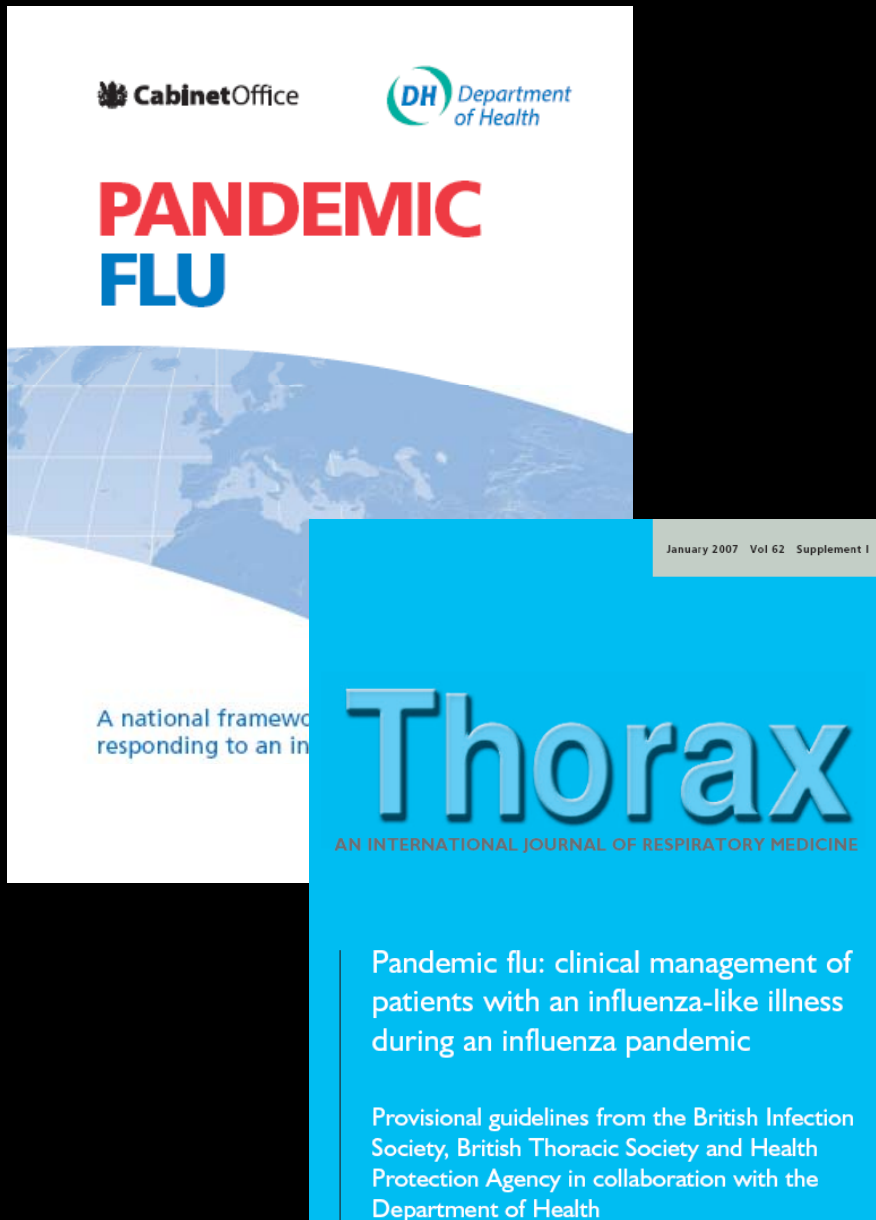
The unique situation of an influenza pandemic



Research Question

Is there enough water in sewage works and the Thames River to dilute projected drug use during an influenza pandemic?

If not, what's the potential impact?



What is Pandemic Preparedness?

... to slow the spread of influenza, through:

1) vaccines,

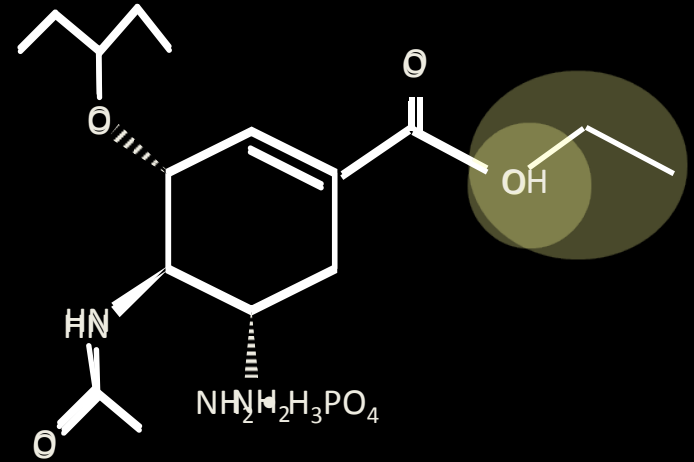
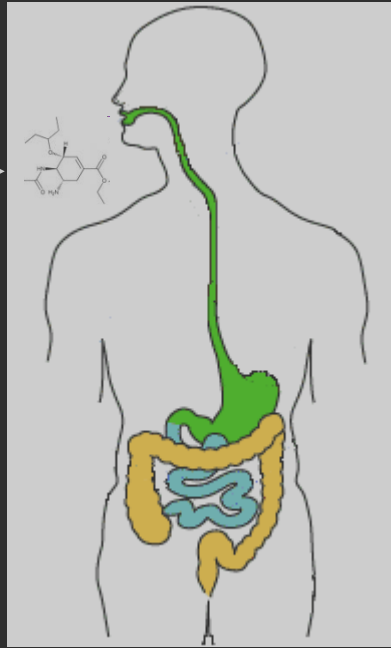
2) non-pharmaceutical measures

3) antivirals



2 x 75 mg/d for 5 days

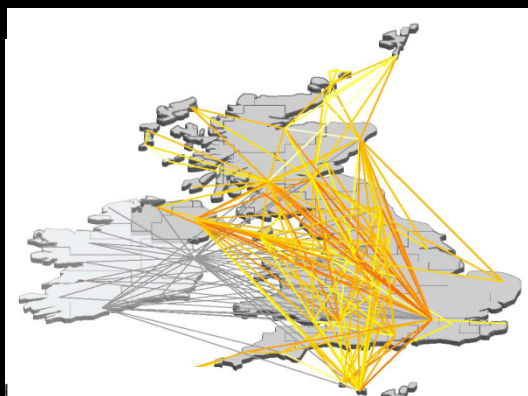
?



Impact Assessment



1. epidemic model



GLEaM – Global Epidemic and Mobility model

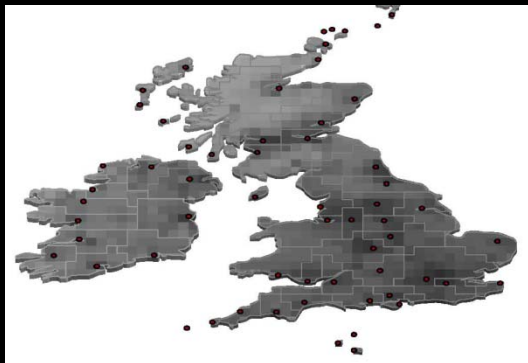
air mobility layer

- 3400 airports in 220 countries
- 20,000 connections
- traffic data (IATA, OAG)
- >99% commercial traffic



commuting mobility layer

- daily commuting data
- >30 countries in 5 continents
- universal law of mobility

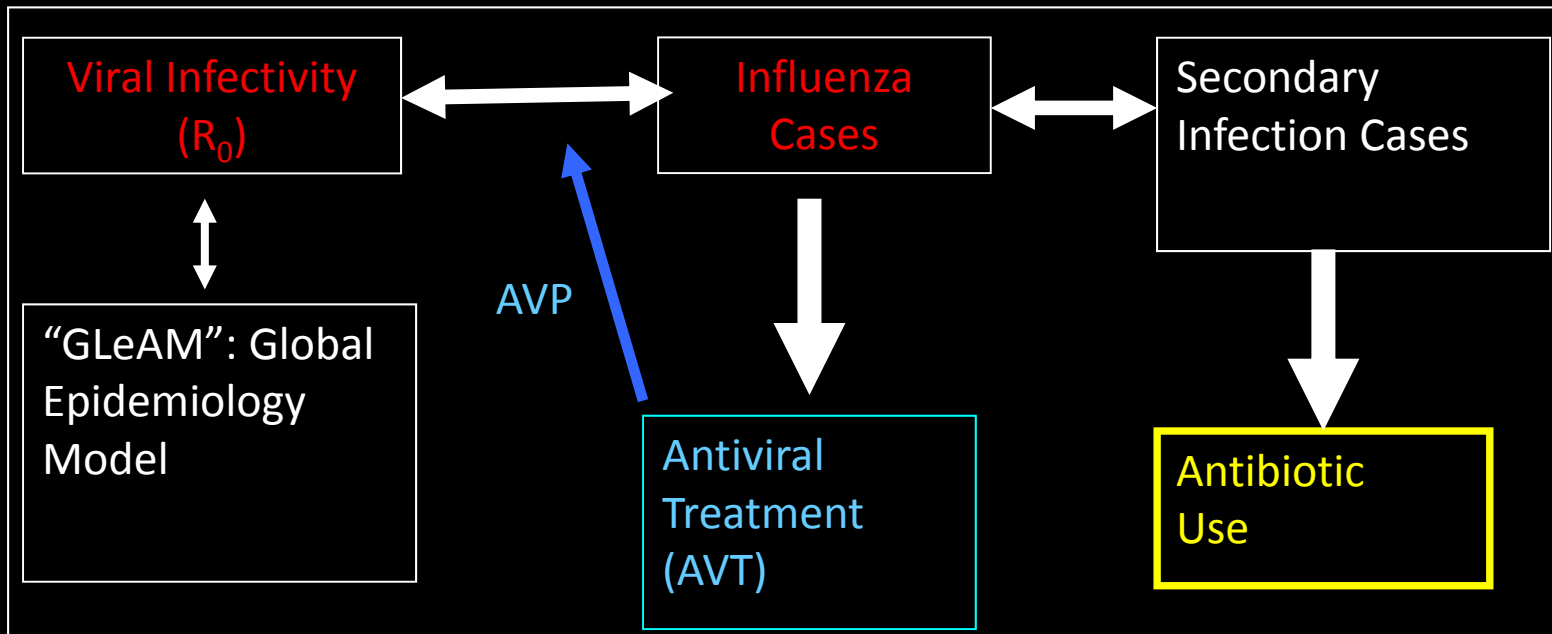


demographic layer

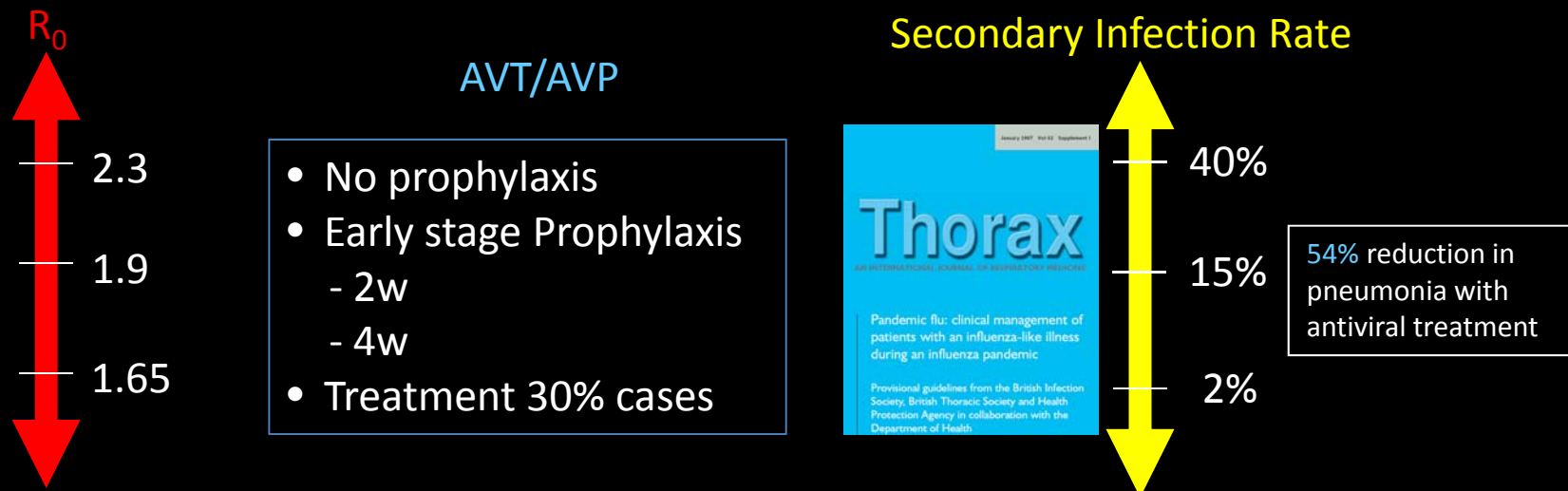
- cells $\frac{1}{4}^\circ \times \frac{1}{4}^\circ$
- tessellation around transportation hubs



Pharmaceutical Use Model During an Influenza Pandemic

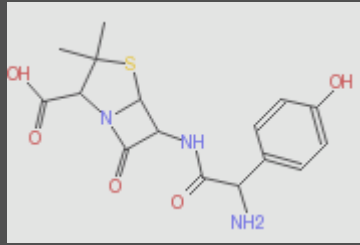


R_0 = number of secondary cases of influenza produced by 1 infected individual

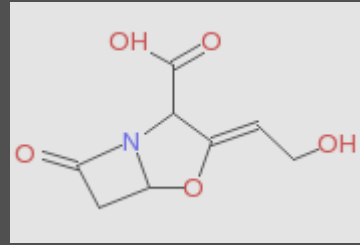
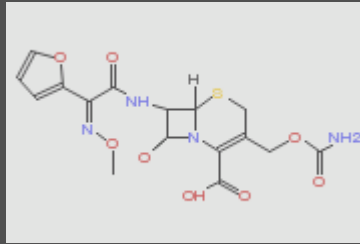


**β-lactam
Cephalosporin**

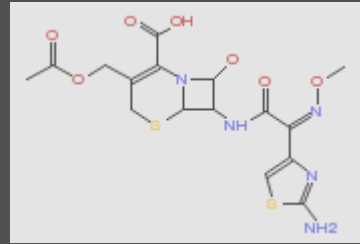
Amoxicillin



Cefuroxime



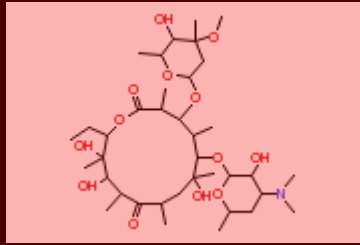
Clavulanic acid



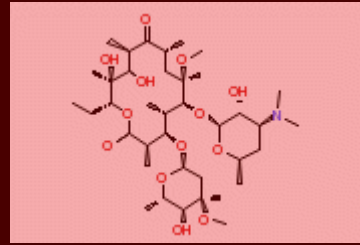
Cefotaxime

Macrolide

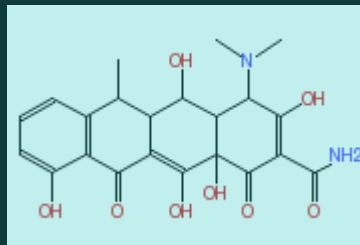
Erythromycin



Clarithromycin



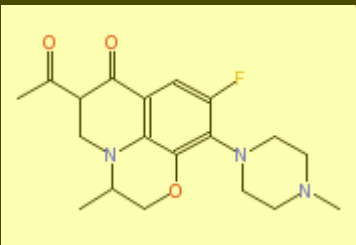
Tetracycline



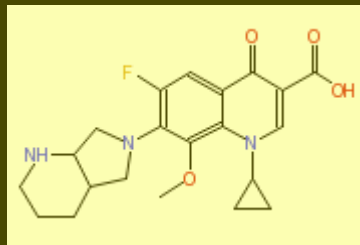
Doxycycline

Quinolone

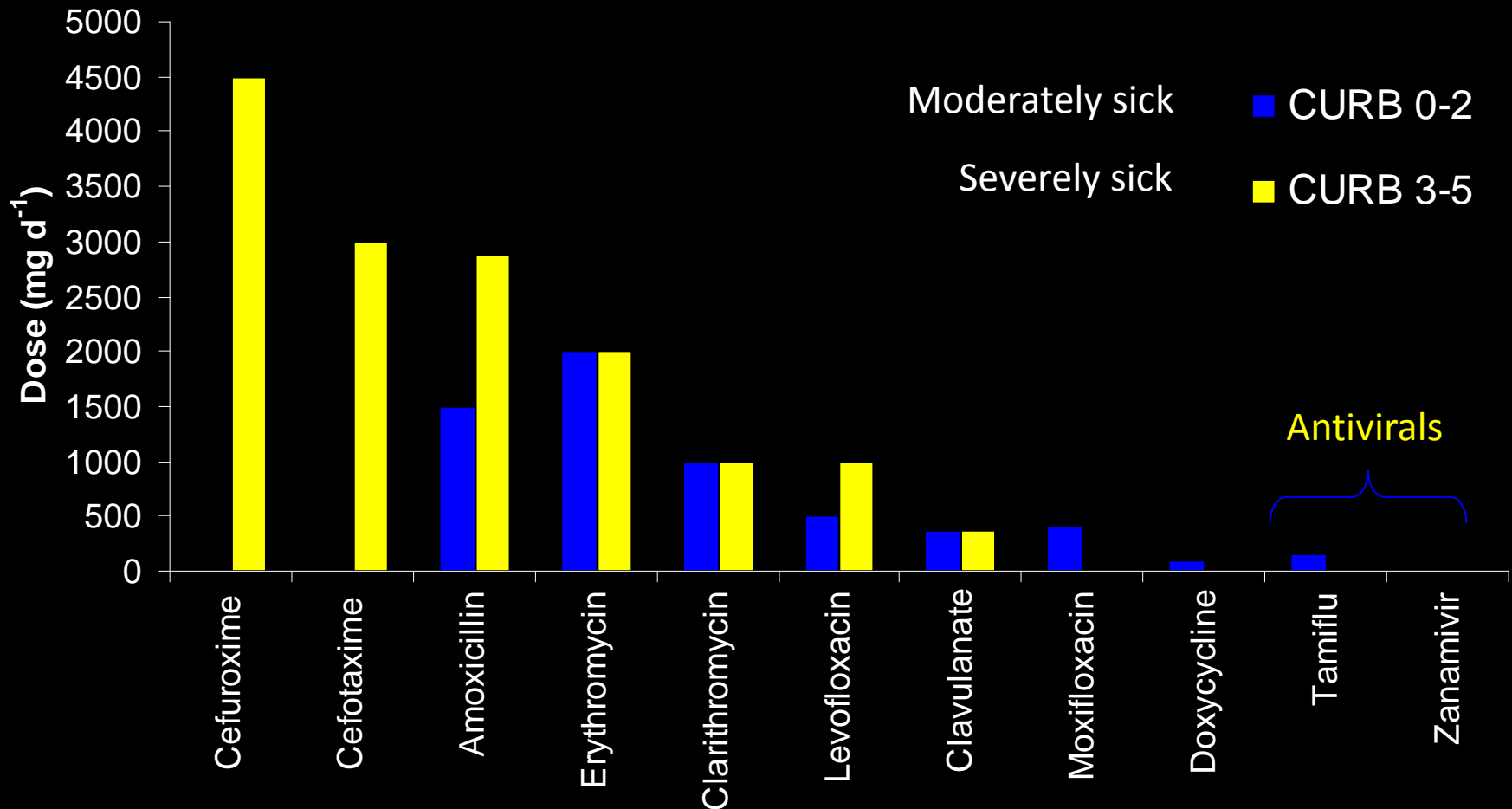
Levofloxacin



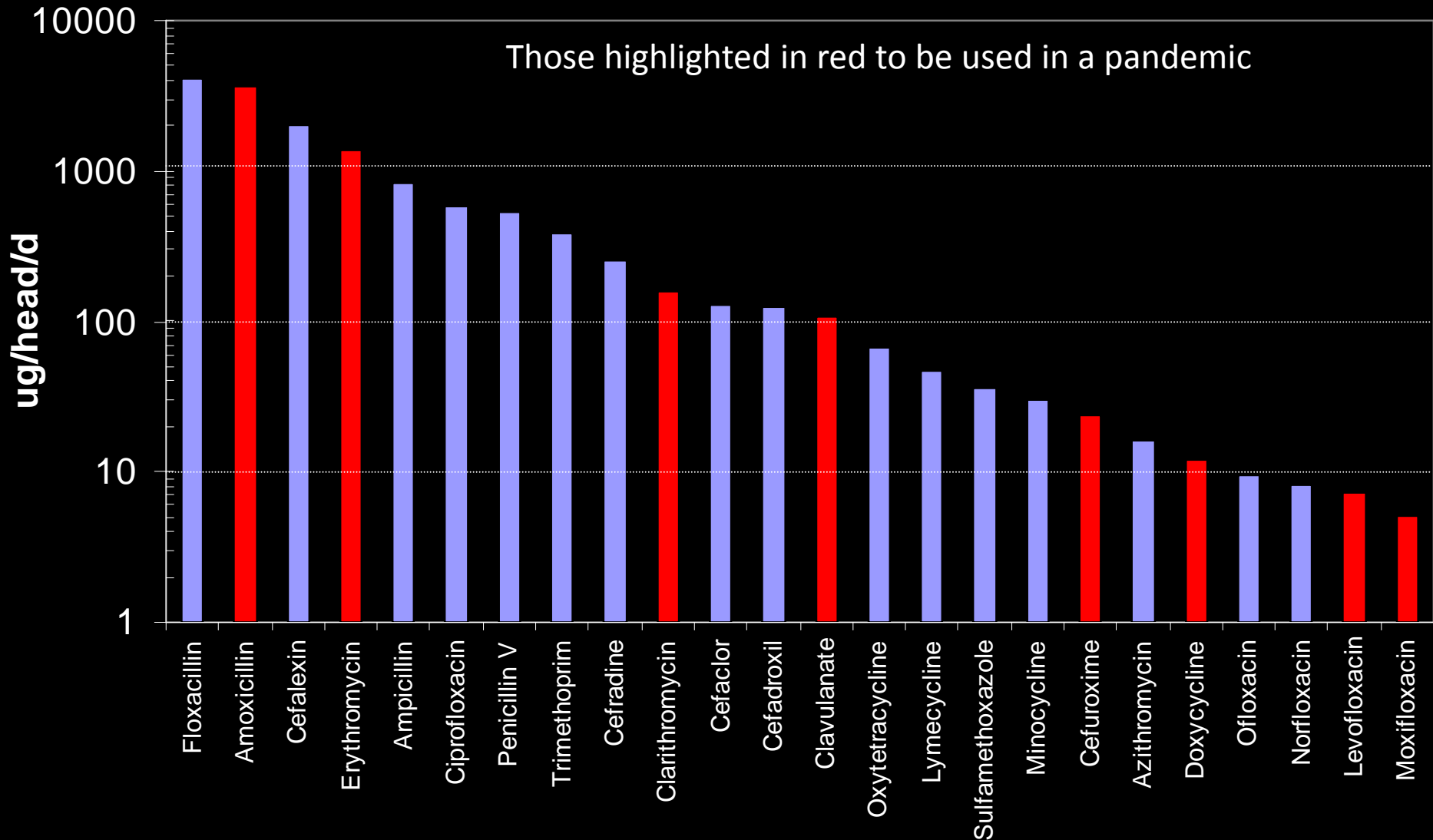
Moxifloxacin



How much will be given to a patient?

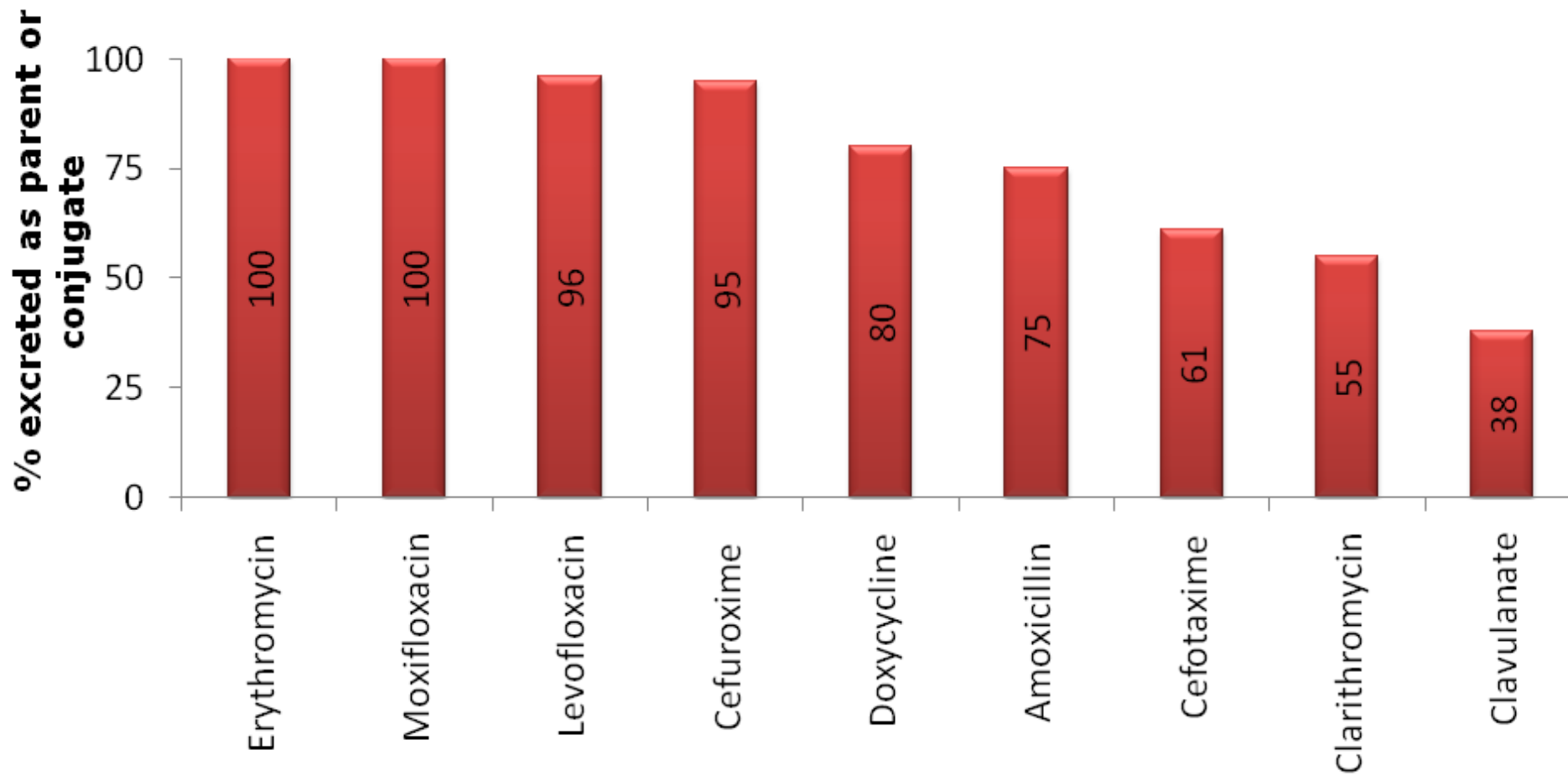


Baseline Antibiotic Use (excreted in England)



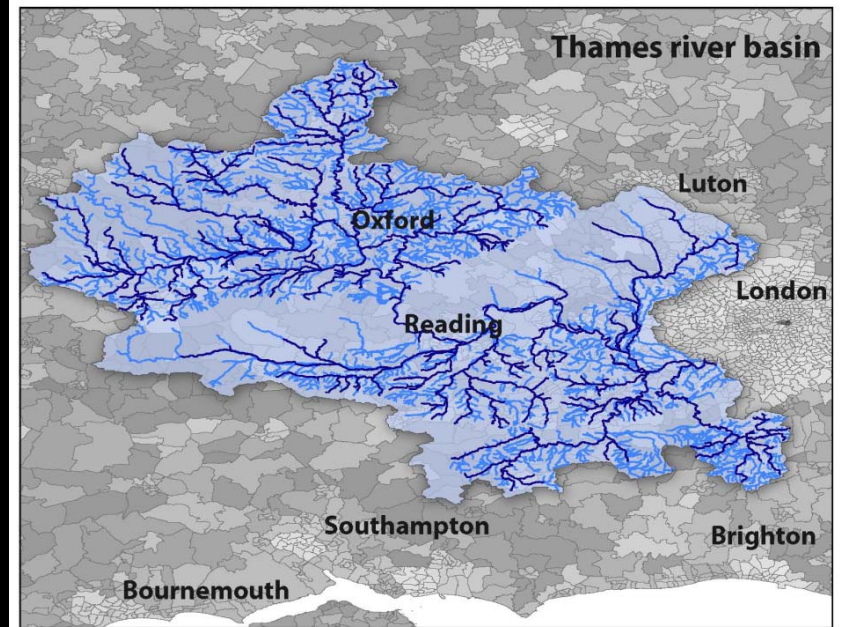
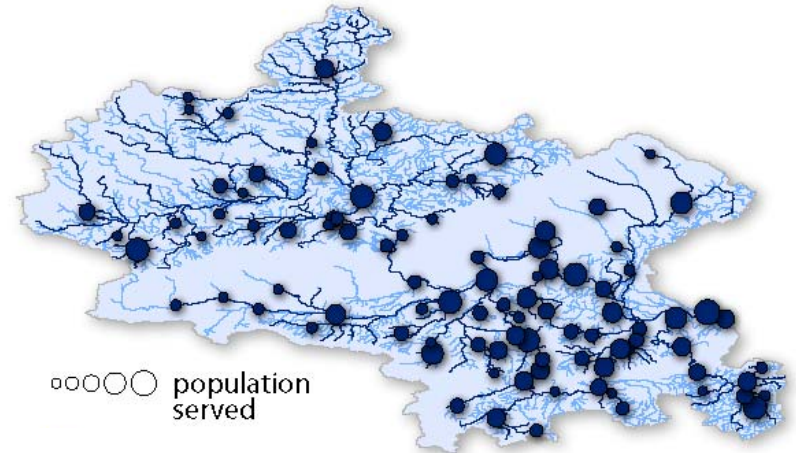


from body to waste

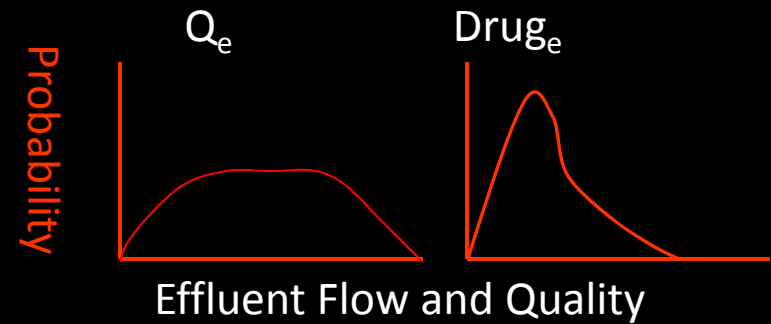
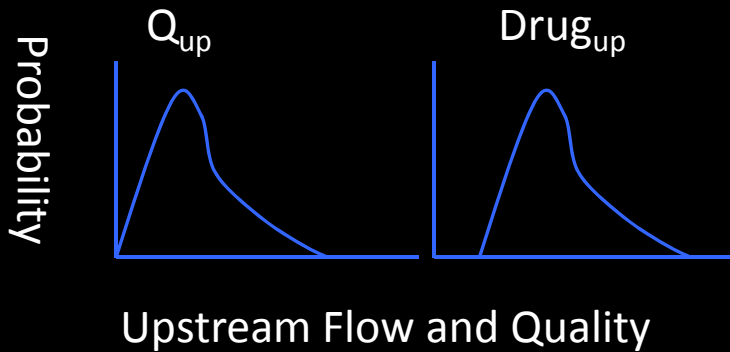


LF2000-WQX works

- Estimates water quality on a reach by reach basis
 - starting at the top
- Makes a mass balance of the inputs to the reach
 - Sewage treatment plants, industrial discharges, tributaries
- New concentrations calculated at the end of the reach allowing for degradation of the compound of interest



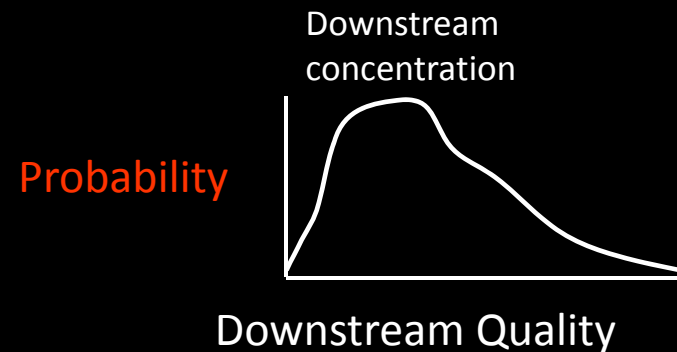
Uses Monte Carlo approach to predict downstream concentrations of contaminant and assign a probability distribution



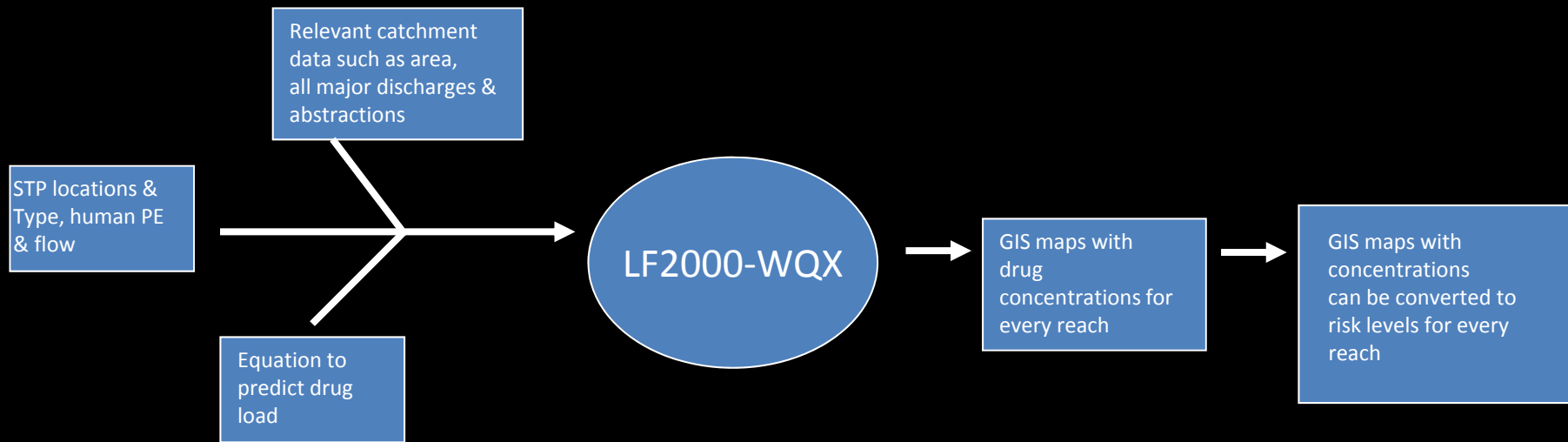
Downstream predicted concentration

Sample from Distributions and do this mass balance calculation many times (shots)

$$Drug\ d = \underbrace{Q_{up} * Drug_{up} + Q_e * Drug_e}_{Q_d}$$



Overview of how model works for a catchment



Determining Impact

Tamiflu



Low projected ecotoxicity
Impact microbial biofilms

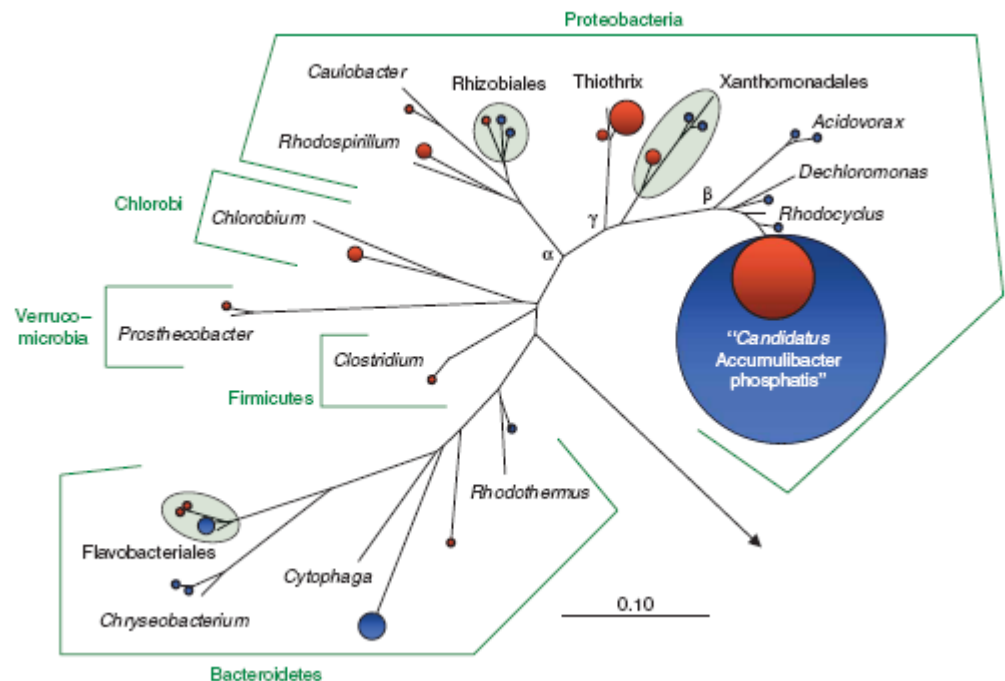
Antibiotics



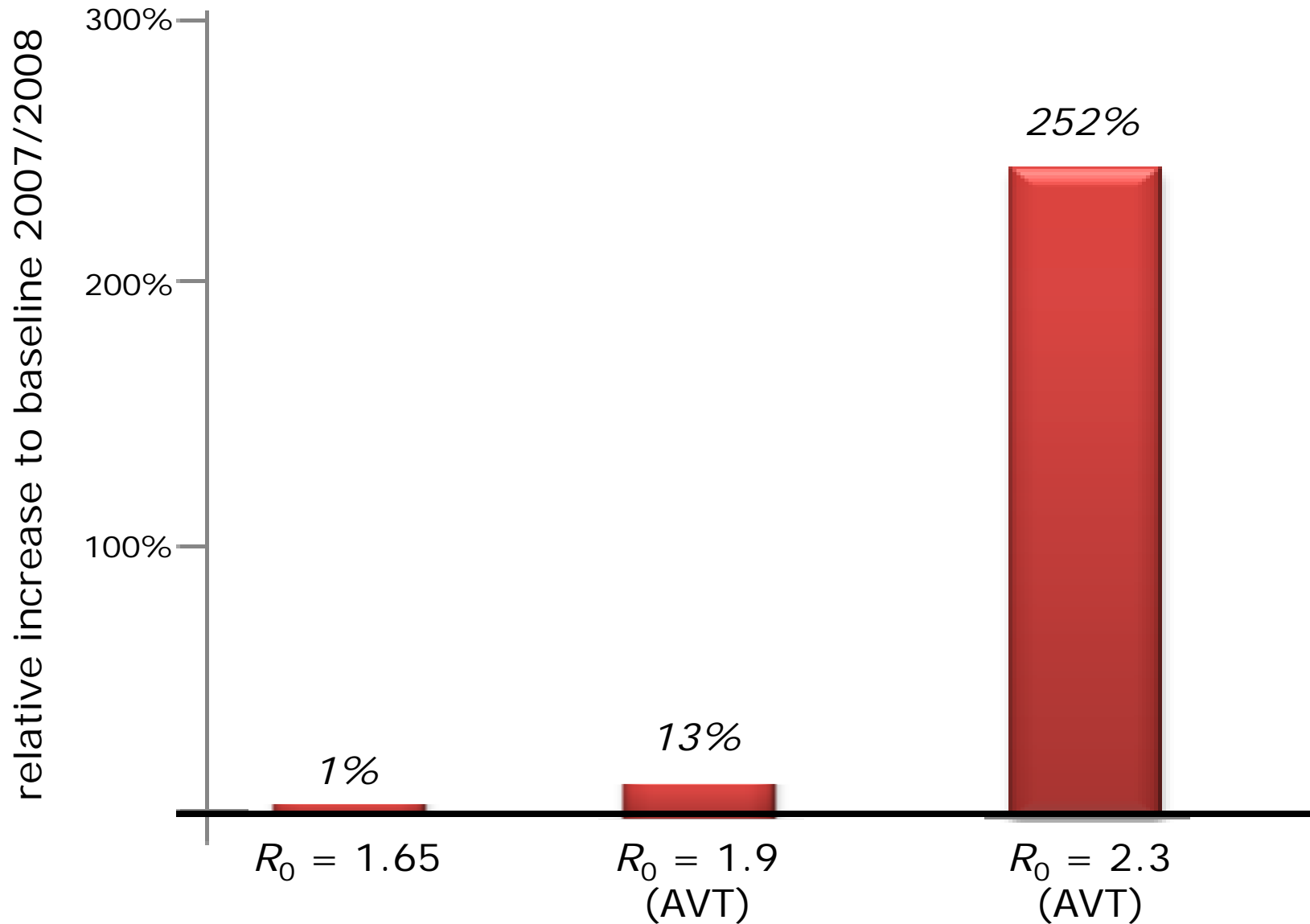
growth inhibition
of microbial species
(WWTP & rivers)

toxicity (0-100%) :

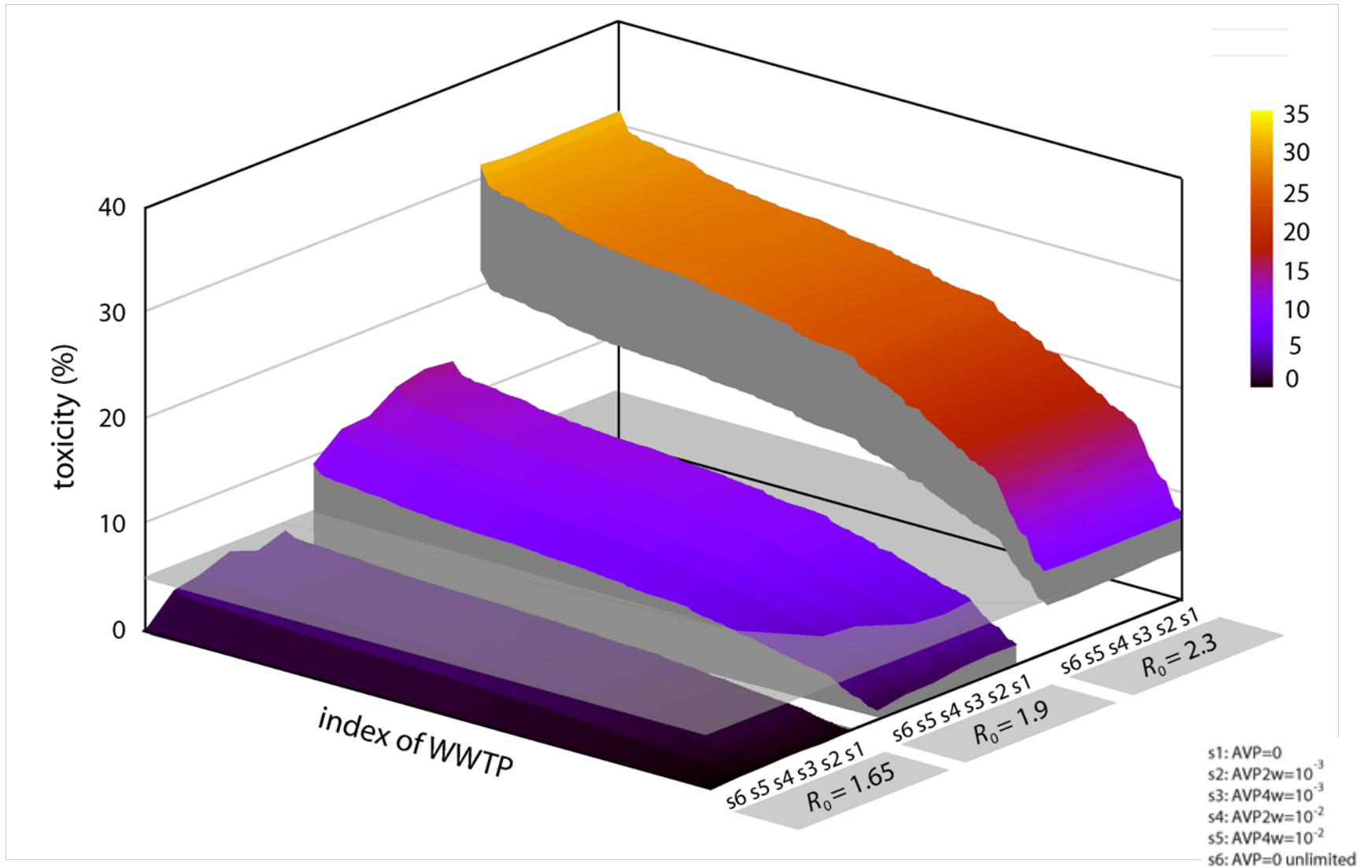
'Potentially affected fraction' of sewage or river microbial species



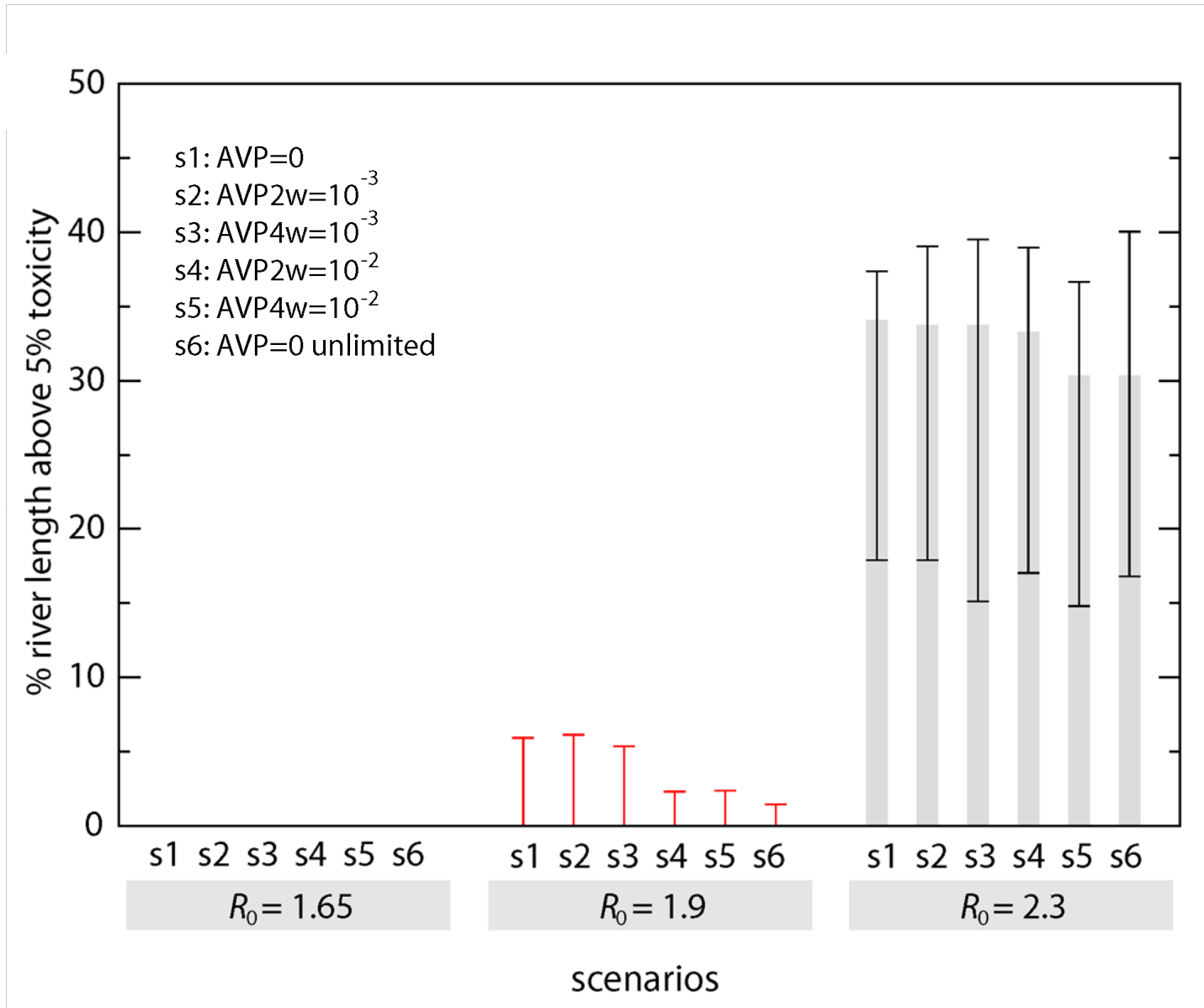
results: antibiotics in WWTPs



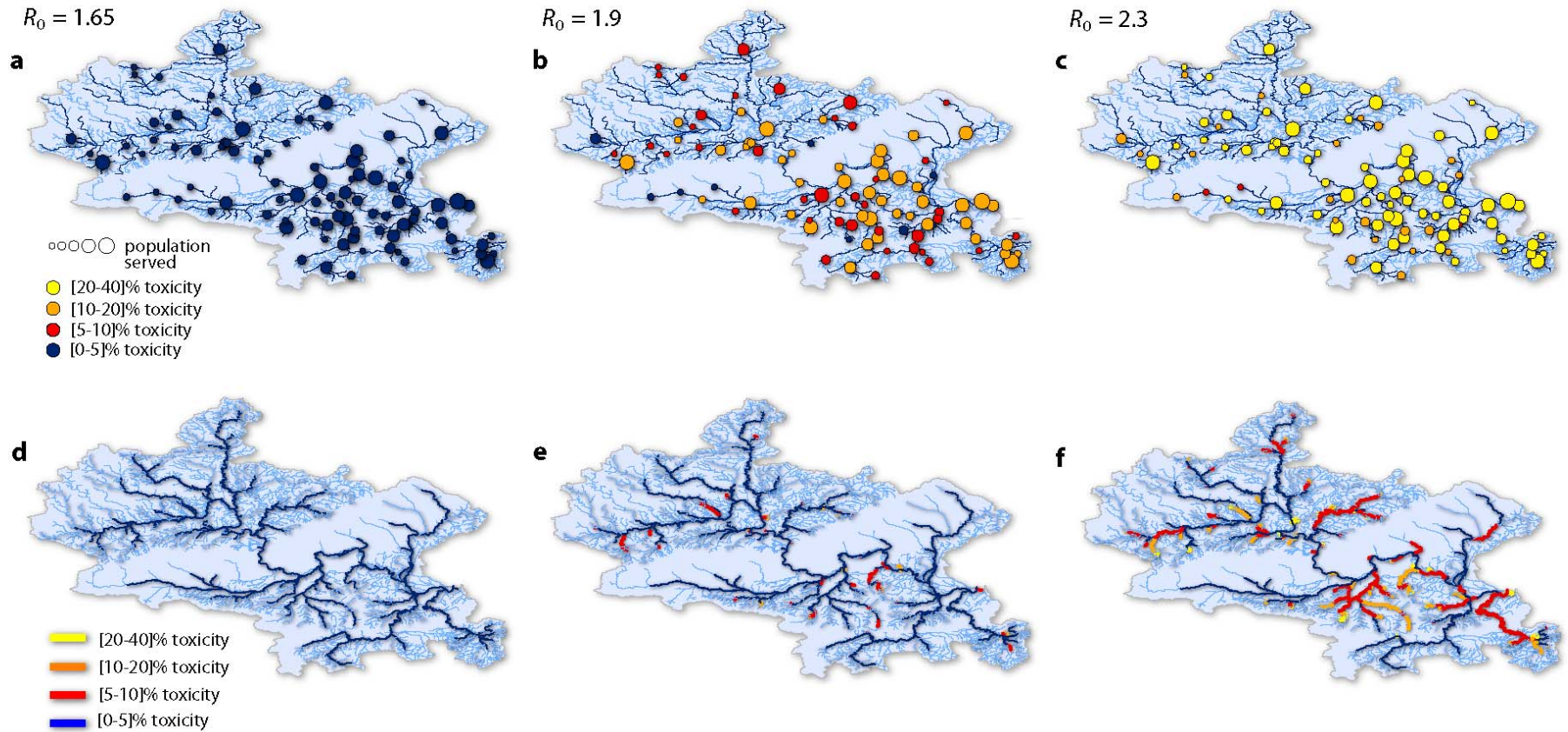
results: toxicity in WWTPs



results: toxicity in rivers (by length)



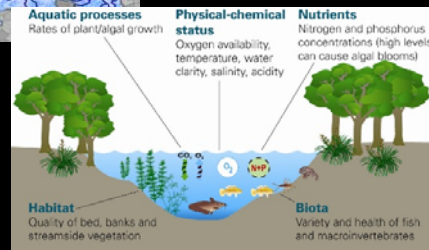
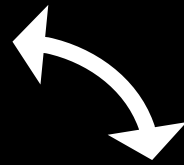
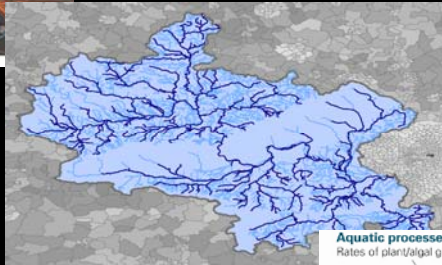
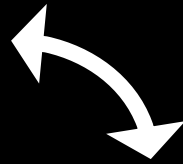
Spatial distribution of toxicity in WWTPs & Rivers



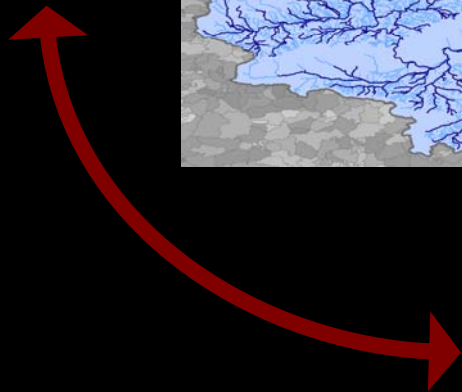
General Conclusions

- A mild pandemic with a low rate of secondary infections is not projected to result in problems for sewage works or most UK rivers.
- A pandemic with an $R_0 > \sim 2.0$ is likely to pose operational challenges to sewage works which could result in the release of untreated sewage into receiving rivers.

Impact



disruption of WWTPs
widespread river pollution



- contamination of rivers
- degradation of drinking water
- spread of **antiviral and antibiotics resistance** leading to:
 - potential loss of key antiviral
 - potential loss of key antibiotics
- eutrophication – leading to:
 - loss of aquatic ecosystem (fish kill)
 - temporary (?) loss of ecosystem function

Solutions ?

VACCINATION!!

Priority Research

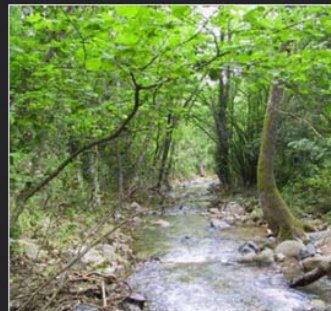
- Empirically determine vulnerability of sewage works.
- Assess the short and long term risks to widespread antiviral and antibiotic release into the environment.
- Empirically determine vulnerability of drinking water to contamination.

Watch this space: www.prepare.org.uk

WELCOME TO PREPARE

PREPARE is a UK Natural Environment Research Council knowledge exchange initiative with the overall aim to integrate the information and expertise required to assess the implications of pharmaceutical usage during a major disease outbreak for the environment, and the risk posed to current wastewater infrastructure.

The PREPARE initiative aims to inform policy, regulation and emergency planning to ensure that ecotoxicologic and human health risks associated with pharmaceutical usage under pandemic and epidemic conditions are thoroughly assessed utilising all and currently available knowledge.



FEATURED ARTICLE

Meeting Report: Risk Assessment of Tamiflu Use Under Pandemic Conditions

Andrew C. Singer,¹ Bruce M. Howard,² Andrew C. Johnson,³ Chris J. Knowles,² Simon Jackman,² Cesare Accinelli,⁴ Anna Barra Caracciolo,⁵ Ian Bernard,² Stephen Bird,⁶ Tatiana Boucard,⁷ Alistair Boxall,⁸ Jayne V. Brian,⁹ Elise Cartmell,¹⁰ Chris Chubb,¹¹ John Churchley,¹² Sandra Costigan,¹³ Mark Crane,¹⁴ Michael J. Dempsey,¹⁵ Bob Dorrington,¹⁶ Brian Ellor,¹⁷ Jerker Fick,¹⁸ John Holmes,¹⁹ Tom Hutchinson,²⁰ Franz Karcher,²¹ Samuel L. Kelleher,¹⁵ Peter Marsden,²² Gerald Noone,²³ Miles A. Nunn,¹ John Oxford,²⁴ Tony Rachwal,²⁵ Noel Roberts,²⁶ Mike Roberts,²⁷ Maria Ludovica Saccà,⁴ Matthew Sanders,²⁸ Jürg Oliver Straub,²⁶ Adrian Terry,²⁹ Dean Thomas,²⁷ Stephen Toovey,²⁶ Rodney Townsend,³⁰ Nikolaos Voulvoulis,³¹ and Chris Watts¹⁴

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[PREPARE]*

Assessing the implications of pharmaceutical release to the environment as a result of a usage during a major disease outbreak

POLICY BRIEFING

Will the medicines used in a flu pandemic mean that sewage treatment plants do not work properly?

At a technical meeting held at Oxford University in November 2007, it was suggested that medicines used during an influenza pandemic might cause disruption to sewage treatment plants to assess the likelihood of this was held on 3rd March 2009. The forum the pharmaceutical industry, water companies, independent organisations involved in forming and implementing public policy. The meeting addressed secondary infections during an influenza pandemic time.

medicines used to treat people during a pandemic age treatment plant performance?

are an essential part of national infrastructure: pathogens and microorganisms that are potentially harmful to human health discharged to the environment. This could affect drinking water supplies in parts of the country where river water flows into the confluence of rivers that are of economic and social value.

An expert meeting at Oxford University addressed the topic

Sewage treatment plants are vital for protecting public health and the

Thanks to Collaborators...and you!

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