



The environmental dimension of antibiotic resistance

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<https://www.exeter.ac.uk/research/amr/>

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European Centre for Environment and
Human Health, Truro



Environment and Sustainability Institute, Penryn

- EDAR group ~20 researchers
- Recent and current funding from NERC, BBSRC, MRC, JPIAMR, DHSC, UKAid
- Focus on environmental microbiomes, but fundamental principles generalisable to human and animal microbiomes



In the 2019-2024 UK strategy there are specific questions highlighted including:

2.3.4 Better understand how AMR spreads between and among humans, animals and the environment

2.4. Minimise spread of AMR through the environment

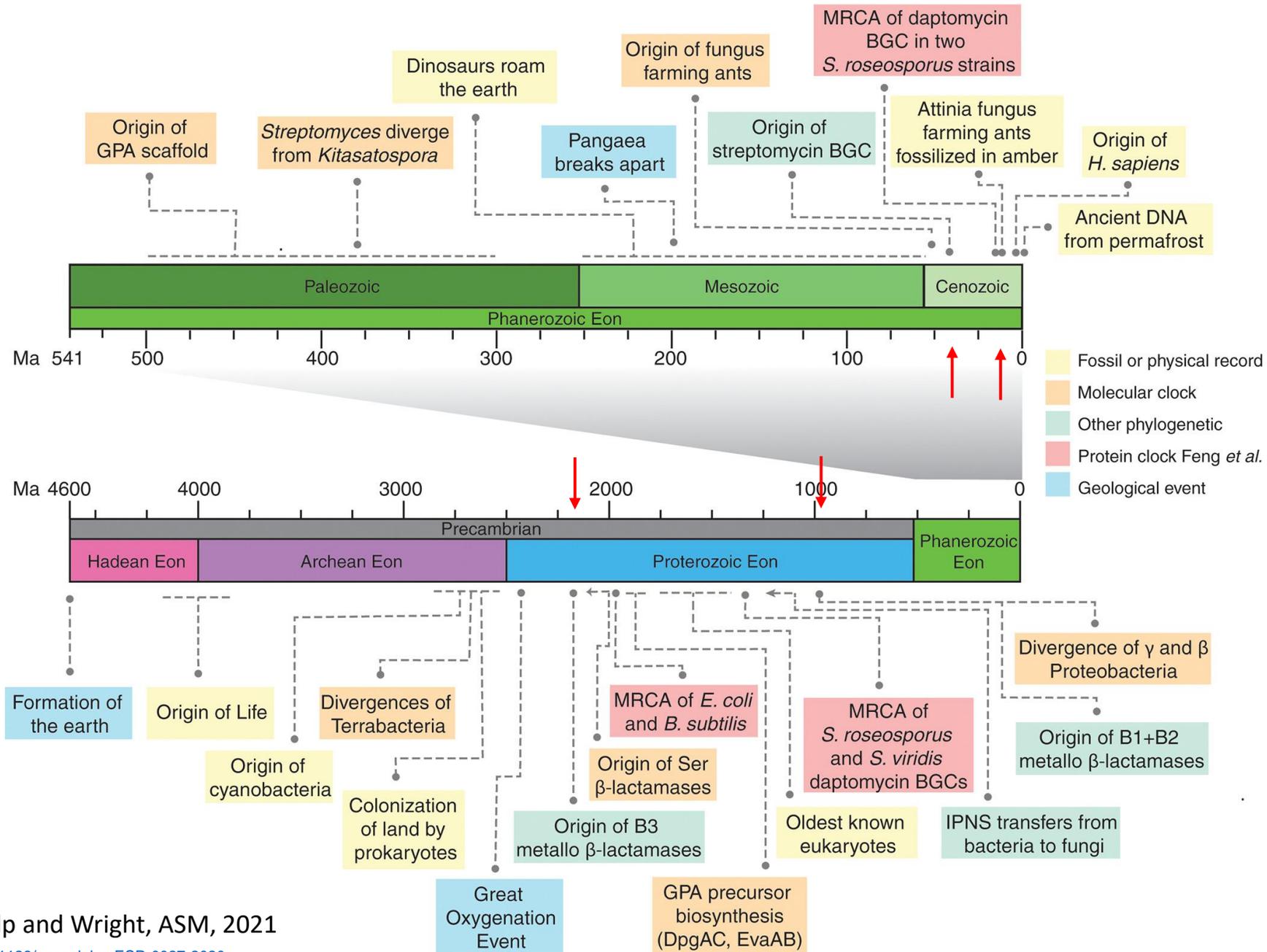
2.4.1 Deepen understanding about AMR in the environment

2.4.2 Minimise antimicrobial contamination

Exeter Environmental Dimension of AMR research programme
uniquely integrates AMR evolution, ecology and transmission



Timeline of antibiotic and resistance development through evolutionary time

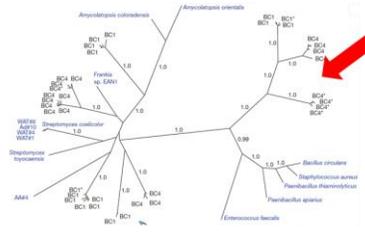


Why the environmental dimension of AMR?

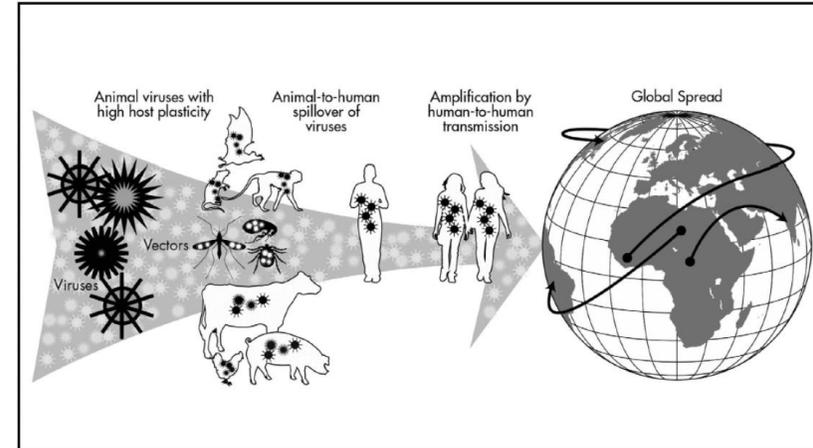
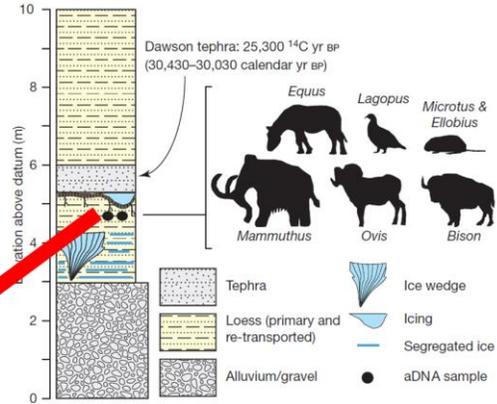
Emergence of AMR

Samples from permafrost before the "Age of Antibiotics"

→ Enormous variety of resistance genes against modern antibiotics



D'Costa et al., 2011, Nature Letters



Acute AMR transmission risk

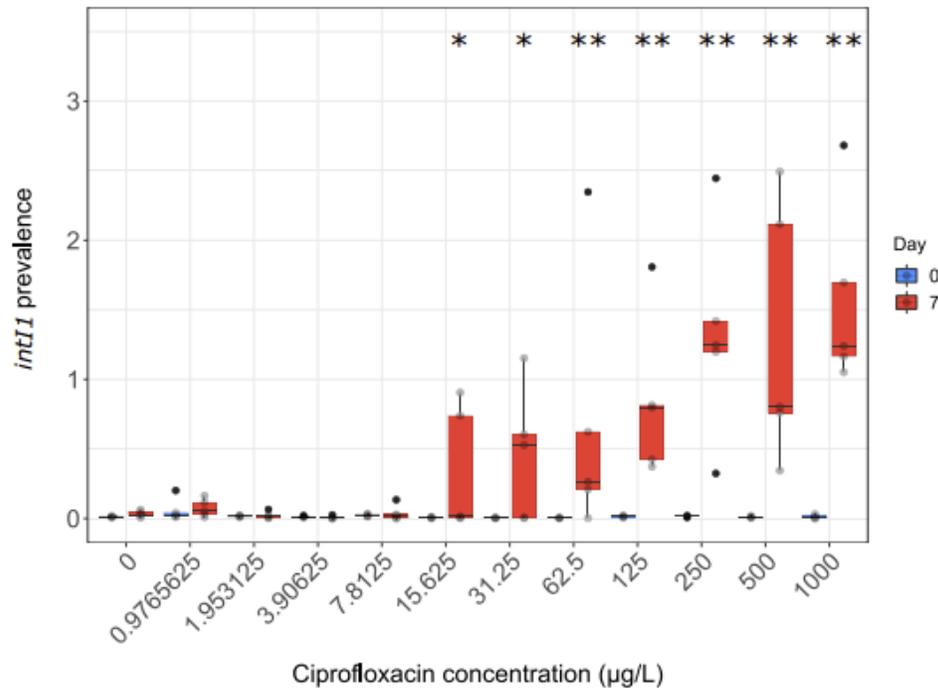


Evolution - role of pharmaceuticals in the environment (and within microbiomes)



Evolution of antibiotic resistance at low antibiotic concentrations including selection below the minimal selective concentration

Isobel C. Stanton¹, Aimee K. Murray¹, Lihong Zhang¹, Jason Snape² & William H. Gaze^{1,3}



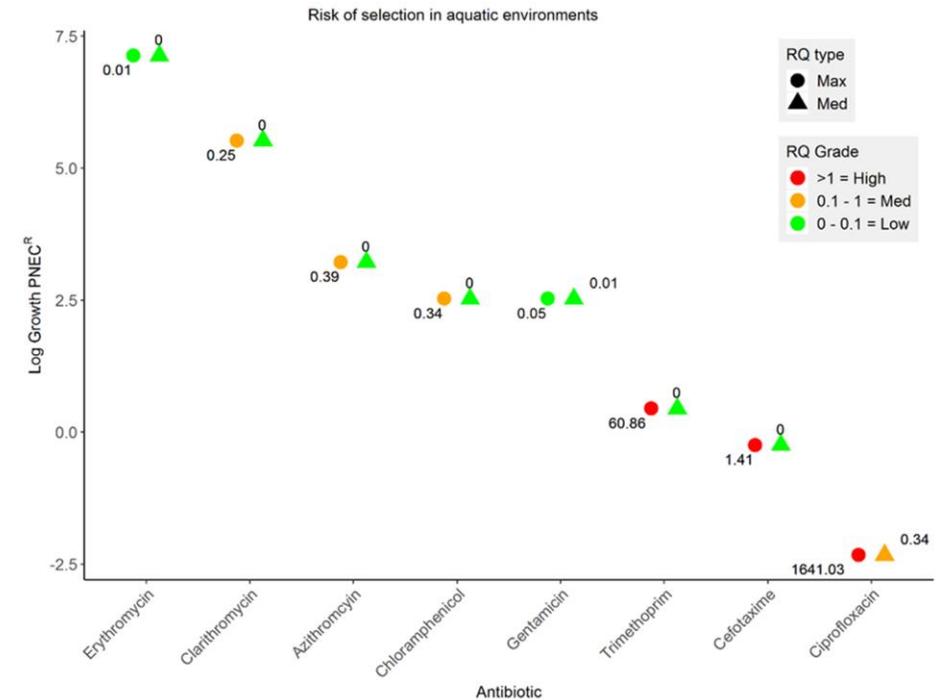
The 'SElection End points in Communities of bacTERia' (SELECT) Method: A Novel Experimental Assay to Facilitate Risk Assessment of Selection for Antimicrobial Resistance in the Environment

Aimee K. Murray,^{1,2} Isobel C. Stanton,^{1,2} Jessica Wright,^{1,2} Lihong Zhang,^{1,2} Jason Snape,³ and William H. Gaze^{1,2}

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Spread of AMR through the environment

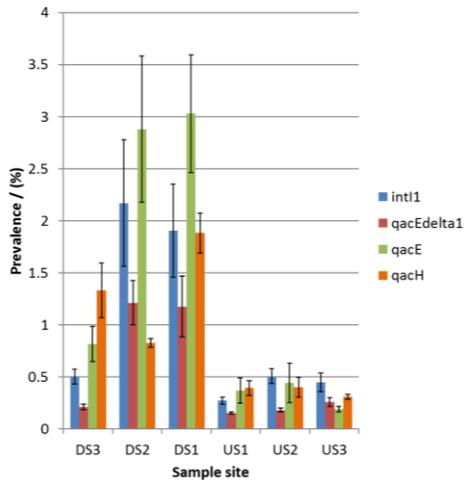
OPEN

ORIGINAL ARTICLE

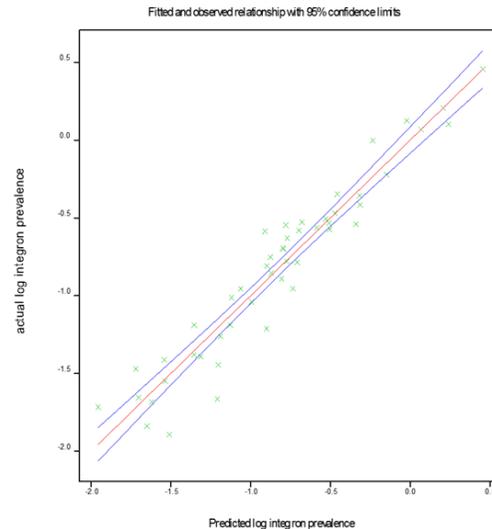
Validated predictive modelling of the environmental resistome

Gregory CA Amos^{1,7}, Emma Gozzard², Charlotte E Carter¹, Andrew Mead^{1,3}, Mike J Bowes², Peter M Hawkey^{4,5}, Lihong Zhang^{1,8}, Andrew C Singer², William H Gaze^{6,9,10} and Elizabeth MH Wellington^{1,9}

The ISME Journal (2015) 9, 1467–1476
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www.nature.com/ismej



model includes WWTP and land use 2km from river



Linear regression models accounted for 82.9 % of the variance seen in log integron prevalence at different sites in the Thames River Basin. 50% of variance associated with point source and 30% with diffuse pollution

Environment International 132 (2019) 105120



Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint



Novel clinically relevant antibiotic resistance genes associated with sewage sludge and industrial waste streams revealed by functional metagenomic screening

L. Zhang^{a,c,s,1}, L. Calvo-Bado^{a,d}, A.K. Murray^c, G.C.A. Amos^{a,e}, P.M. Hawkey^b, E.M. Wellington^a, W.H. Gaze^{a,c,1}



American Society for Microbiology
Antimicrobial Agents and Chemotherapy
Volume 60, Issue 10, October 2016, Pages 5828-5840
<https://doi.org/10.1128/AAC.00750-16>

Mechanisms of Resistance

Structural and Biochemical Characterization of Rm3, a Subclass B3 Metallo- β -Lactamase Identified from a Functional Metagenomic Study

Ramya Salimraj^a, Lihong Zhang^{b,*}, Philip Hinchliffe^a, Elizabeth M. H. Wellington^b, Jürgen Brem^c, Christopher J. Schofield^c, William H. Gaze^{b,*}, and James Spencer^a



Environmental transmission

Environment International 82 (2015) 92–100



Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint



Human recreational exposure to antibiotic resistant bacteria in coastal bathing waters

Anne F.C. Leonard, Lihong Zhang, Andrew J. Balfour, Ruth Garside, William H. Gaze *

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6 million recreational sessions occurred in 2012 in England and Wales that resulted in the ingestion of 3GC resistant *E. coli*.

Tackling antimicrobial resistance 2019–2024

AMR IN THE WATER

The scale and complexity of AMR contamination of aquatic environments is widely recognised, and a subject of much study. In the past five years, almost 1000 research papers were published on AMR and the water environment. There is no question that antibiotics can be found in both final effluents and in rivers downstream of sewage treatment plants.

As the volume of academic study expands, scientists have begun to reveal the role of the environment as a pathway for humans to pollute the environment and both acquire and develop AMR.

In 2015, researchers found the first link between environmental exposure of people in British coastal waters and colonisation by resistant bacteria². Surfers in the sea exposed to resistant organisms from sewage treatment works were found to carry resistant bacteria of the same genotype as those in the plants.

Exposure to and colonisation by antibiotic-resistant *E. coli* in UK coastal water users: Environmental surveillance, exposure assessment, and epidemiological study (Beach Bum Survey)

Anne F.C. Leonard^{a,*}, Lihong Zhang^{a,*}, Andrew J. Balfour^a, Ruth Garside^a, Peter M. Hawkey^b, Aimee K. Murray^a, Obioha C. Ukoumunne^c, William H. Gaze^{a,*}

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^c National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care South West Peninsula, University of Exeter Medical School, Exeter EX1 2LU, UK



Surfers were ~3 times as likely to be colonised by 3rd generation cephalosporin resistant *E. coli* than non surfers

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doi: 10.2903/j.efsa.2021.6651

Role played by the environment in the emergence and spread of antimicrobial resistance (AMR) through the food chain

EFSA Panel on Biological Hazards (BIOHAZ),
Konstantinos Koutsoumanis, Ana Allende, Avelino Álvarez-Ordóñez, Declan Bolton,
Sara Bover-Cid, Marianne Chemaly, Robert Davies, Alessandra De Cesare, Lieve Herman,
Friederike Hilbert, Roland Lindqvist, Maarten Nauta, Giuseppe Ru, Marion Simmons,
Panagiotis Skandamis, Elisabetta Suffredini, Héctor Argüello, Thomas Berendonk,
Lina Maria Cavaco, William Gaze, Heike Schmitt, Ed Topp, Beatriz Guerra, Ernesto Liébana,
Pietro Stella and Luisa Peixe

<https://www.efsa.europa.eu/en/efsajournal/pub/6651>



FRONTIERS 2017

Emerging Issues of Environmental Concern



Frontiers 2017: Emerging Issues of Environmental Concern

The Frontiers 2017 report presents six emerging issues of environmental concern with global implications. The report highlights emerging challenges for decision makers from government, business and civil society and provides them with the knowledge and options to act quickly. Download the report [here](#).

<https://www.unep.org/resources/frontiers-2017-emerging-issues-environmental-concern>



<https://wellcome.org/sites/default/files/antimicrobial-resistance-environment-report.pdf>



JRC TECHNICAL REPORT

Selection of substances for the 3rd Watch List under the Water Framework Directive

Luisa Gomez-Corcos, Dimitar Menev, Isabella Sansonetti,
Ana Beatriz Garcia, Magdalena Negredo, Elena Perez
Rodriguez, and Tamas Letellier



https://images.chemycal.com/Media/Files/third_watch_list_report_pdf.pdf



How do we evaluate the significance of the environment in the knowledge that -

1. Gene transfer from environmental bacteria leads to emergence of novel resistance genes in human and animal pathogens
2. Due to co-selection associated with genetic complexity all antimicrobials have the potential to drive the emergence of clinically important resistance genes
3. Mobile AMR genes have independent evolutionary trajectories to their bacterial hosts - even within a hospital setting resistance genes are mobilised between host and plasmid type over short time frames (Sheppard et al., 2017)
4. The fact that most transmission of clinical pathogens may occur from person - person doesn't reduce the importance of HGT from environmental bacteria to human commensals/pathogens
5. Environmental transmission from human faecal pollution will be indistinguishable from human – human community transmission using conventional epidemiological approaches



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now at Dresden

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Dr Ed Topp (AAF Canada)

