Edinburgh Infectious Diseases

IS THERE A LINK BETWEEN ANTIBIOTIC USAGE IN LIVESTOCK AND AMR IN HUMAN PATIENTS?

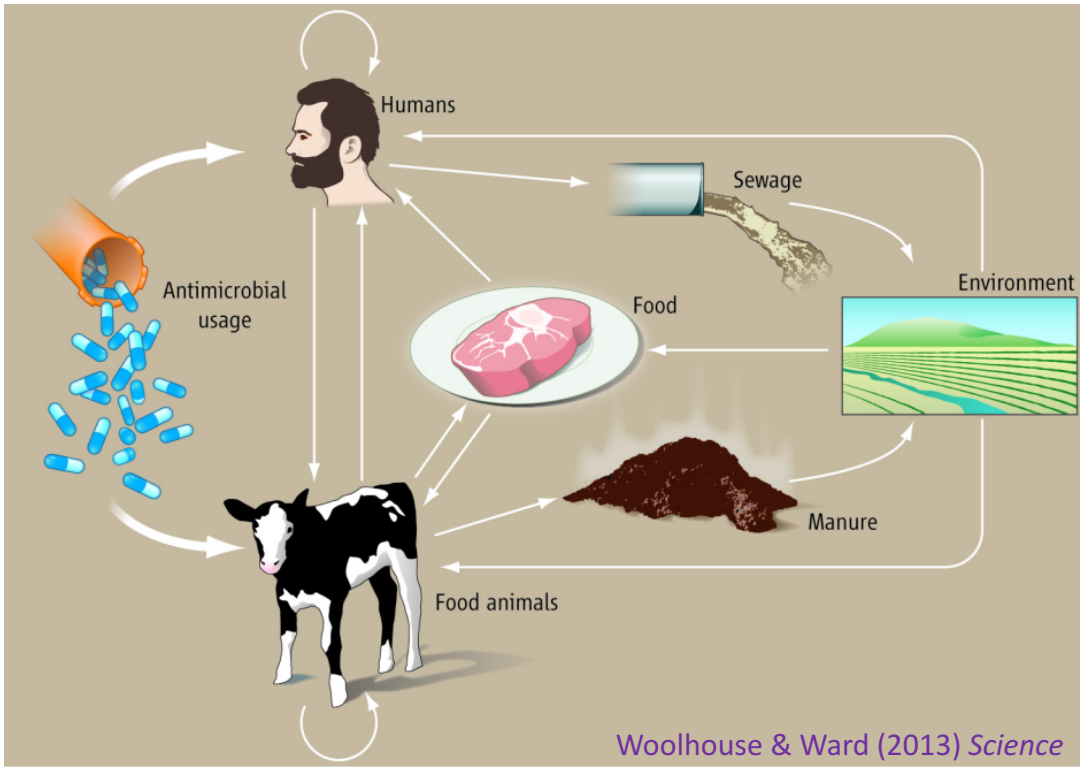
Mark Woolhouse

Edinburgh Infectious Diseases

SULSA
Scottish Universities Life Sciences Alliance

Antimicrobial Resistance Conference
Thursday 26 – Friday 27 April 2018

AMR IS A ONE HEALTH ISSUE



Multiple modes of movement:

- bacteria
- mobile genetic elements
- drug residues

Multiple drug-bug combinations

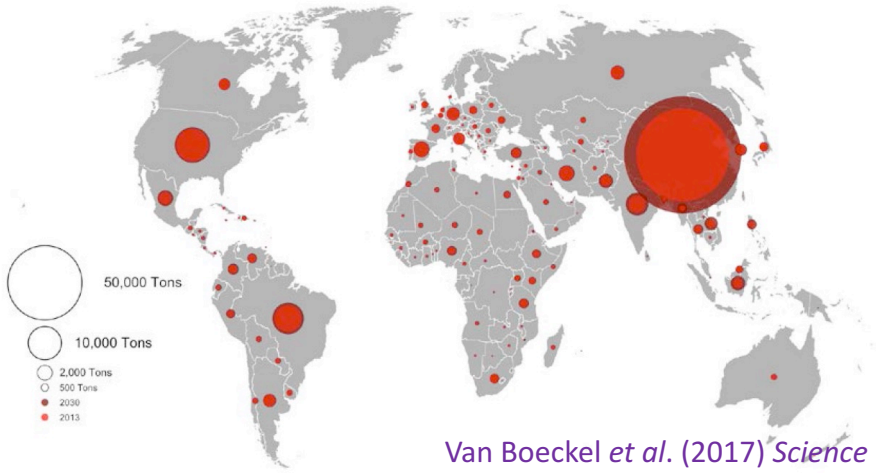
"When you can measure what you are speaking about and express it in numbers, you know something about it, but when you cannot express it in numbers your knowledge about it is of a meagre and unsatisfactory kind"

Lord Kelvin (1883)

ANTIBIOTICS ON THE FARM

- Industrial agriculture works with very small margins

- Antibiotics used as:
  - metaphylaxis
  - prophylaxis
  - growth promoters



Van Boeckel *et al*. (2017) *Science*

- Antibiotic usage in livestock:humans ≈ 1:1 globally

RESISTANCE ON THE FARM

APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Nov. 2005, p. 6680–6688 Vol. 71, No. 11
0099-2240/05/$08.00+0 doi:10.1128/AEM.71.11.6680–6688.2005

Molecular Epidemiology of Antimicrobial-Resistant Commensal *Escherichia coli* Strains in a Cohort of Newborn Calves

Deborah V. Hoyle,[1,2] Catherine M. Yates,[2] Margo E. Chase-Topping,[1]* Esther J. Turner,[2] Sarah E. Davies,[2] J. Chris Low,[3] George J. Gunn,[3] Mark E. J. Woolhouse,[1] and Sebastian G. B. Amyes[2]

Available online at www.sciencedirect.com
SCIENCE DIRECT
ELSEVIER
Veterinary Microbiology 115 (2006) 250–257
veterinary microbiology
www.elsevier.com/locate/vetmic

Short communication

Molecular characterisation of bovine faecal *Escherichia coli* shows persistence of defined ampicillin resistant strains and the presence of class 1 integrons on an organic beef farm

D.V. Hoyle [a,b], H.C. Davison [c], H.I. Knight [d], C.M. Yates [a], O. Dobay [a,e], G.J. Gunn [d], S.G.B. Amyes [a], M.E.J. Woolhouse [f,*]

Journal of Antimicrobial Chemotherapy (2004) **54**, 534–537
DOI: 10.1093/jac/dkh353
Advance Access publication 1 July 2004
JAC

High frequency transfer and horizontal spread of apramycin resistance in calf faecal *Escherichia coli*

C. M. Yates[1]*, M. C. Pearce[2], M. E. J. Woolhouse[2] and S. G. B. Amyes[1]

Journal of Antimicrobial Chemotherapy (2004) **53**, 867–871
DOI: 10.1093/jac/dkh177
Advance Access publication 31 March 2004
JAC

Acquisition and epidemiology of antibiotic-resistant *Escherichia coli* in a cohort of newborn calves

Deborah V. Hoyle[1], Hazel I. Knight[1,2], Darren J. Shaw[1]*, Kevin Hillman[3], Michael C. Pearce[1,2], J. Chris Low[4], George J. Gunn[2] and Mark E. J. Woolhouse[1]

APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Nov. 2004, p. 6927–6930 Vol. 70, No. 11
0099-2240/04/$08.00+0 DOI: 10.1128/AEM.70.11.6927–6930.2004

Age-Related Decline in Carriage of Ampicillin-Resistant *Escherichia coli* in Young Calves

Deborah V. Hoyle,[1,2]* Darren J. Shaw,[1] Hazel I. Knight,[1,3] Helen C. Davison,[4] Michael C. Pearce,[1,3] J. Chris Low,[5] George J. Gunn,[3] and Mark E. J. Woolhouse[1]

biology letters
Biol. Lett. (2006) 2, 463–465
doi:10.1098/rsbl.2006.0478
Published online 18 April 2006

Enhancement of bacterial competitive fitness by apramycin resistance plasmids from non-pathogenic *Escherichia coli*

C. M. Yates[1,*], D. J. Shaw[2], A. J. Roe[1], M. E. J. Woolhouse[3] and S. G. B. Amyes[1]

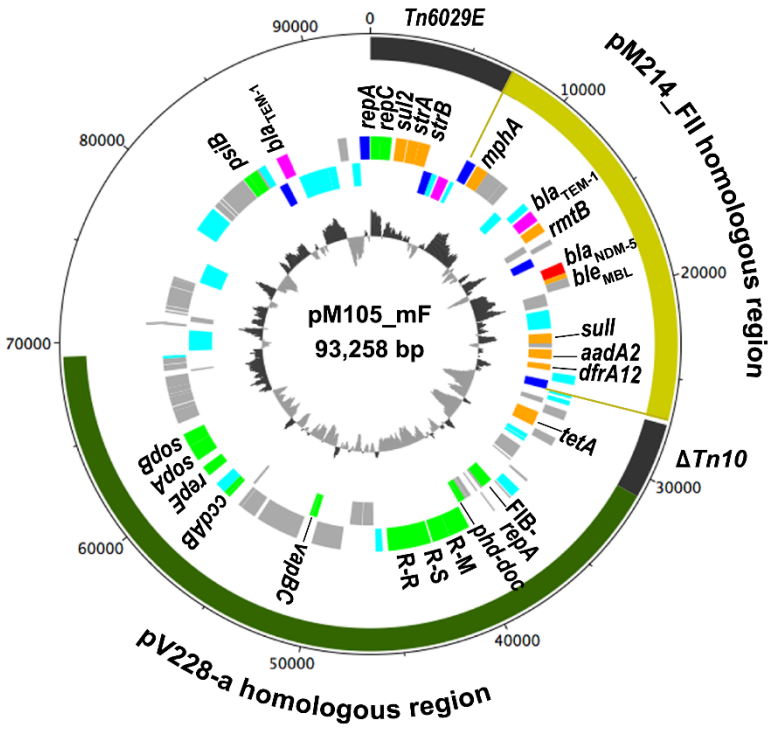
J Antimicrob Chemother 2013
doi:10.1093/jac/dks393
Advance Access publication 2 October 2012

Salmonella enterica subsp. *enterica* producing VIM-1 carbapenemase isolated from livestock farms

Jennie Fischer[1], Irene Rodríguez[1], Silvia Schmoger[1], Anika Friese[2], Uwe Roesler[2], Reiner Helmuth[1] and Beatriz Guerra[1]*

WHAT'S THE RISK?

Resistant food-borne infections account for up to:
1 in 5 illnesses
<1 in 300 deaths
out of total AMR burden



Sugawara *et al*. (2017) *PNAS*

WHAT'S THE RISK?

Risk Analysis, Vol. 26, No. 1, 2006 DOI: 10.1111/j.1539-6924.2006.00723.x

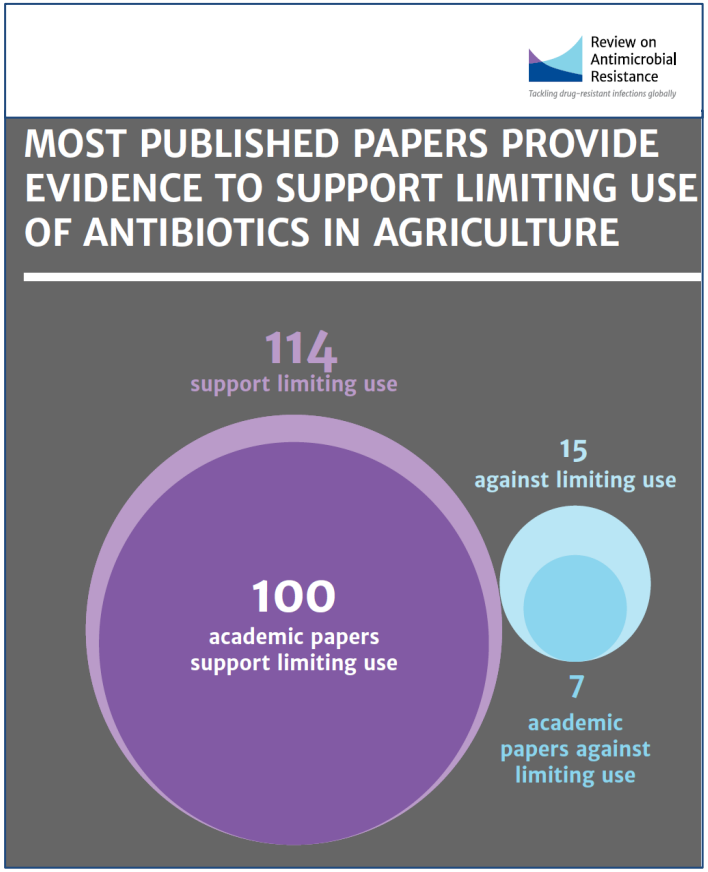
Quantifying Potential Human Health Impacts of Animal Antibiotic Use: Enrofloxacin and Macrolides in Chickens

Louis Anthony (Tony) Cox, Jr.[1]* and Douglas A. Popken[1]

Use of similar or identical antibiotics in both human and veterinary medicine has come under increasing scrutiny by regulators concerned that bacteria resistant to animal antibiotics will infect people and resist treatment with similar human antibiotics, leading to excess illnesses and deaths. Scientists, regulators, and interest groups in the United States and Europe have urged bans on nontherapeutic and some therapeutic uses of animal antibiotics to protect human health. Many regulators and public health experts have also expressed dissatisfaction with the perceived limitations of quantitative risk assessment and have proposed alternative qualitative and judgmental approaches ranging from "attributable fraction" estimates to risk management recommendations based on the precautionary principle or on expert judgments
dicine. This article presents a
n health impacts of continuing
production of broiler chickens
d applied to available data. It
re human illness-days than it
atio for human health impacts
es. This conclusion is driven by
ntibiotic use increases illnesses
imals, and hence human health
sessment for animal antibiotics

Withdrawing animal antibiotics can cause far more human illness-days than it would prevent: the estimate human benefit:risk ratio… exceeds 1000:1 in many cases.

WHAT'S THE EVIDENCE?



WHAT'S THE EVIDENCE?

Restricting the use of antibiotics in food-producing animals and its associations with antibiotic resistance in food-producing animals and human beings: a systematic review and meta-analysis

Karen L Tang, Niamh P Caffrey, Diego B Nóbrega, Susan C Cork, Paul E Ronksley, Herman W Barkema, Alicia J Polachek, Heather Ganshorn, Nishan Sharma, James D Kellner, William A Ghali

Lancet Planet Health 2017

Published Online
November 6, 2017
http://dx.doi.org/10.1016/S2542-5196(17)30141-9

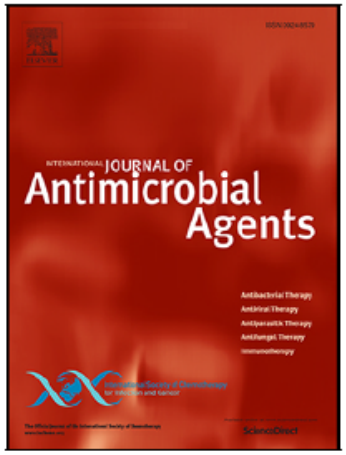
See Online/Comment
http://dx.doi.org/10.1016/S2542-5196(17)30142-0

Accepted Manuscript

Is antimicrobial administration to food animals a direct threat to human health? A rapid systematic review.

Anna Mae Scott , Elaine Beller , Paul Glasziou , Justin Clark , Respati W. Ranakusuma , Oyungerel Byambasuren , Mina Bakhit , Stephen W. Page , Darren Trott , Chris Del Mar

PII: S0924-8579(18)30107-9
DOI: 10.1016/j.ijantimicag.2018.04.005
Reference: ANTAGE 5420



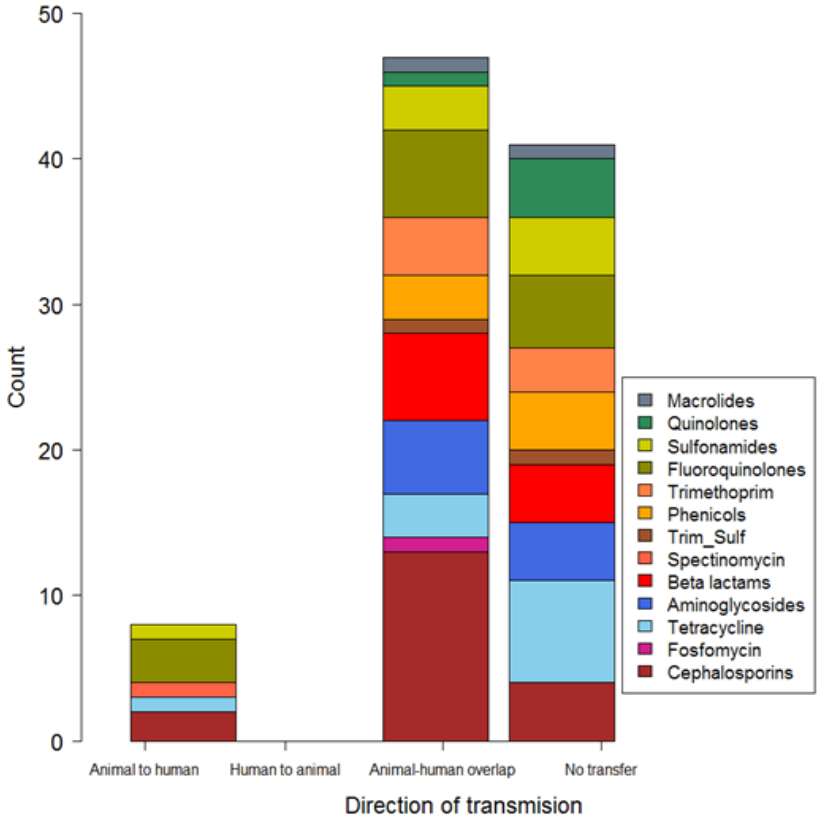
WHAT'S THE EVIDENCE?

Systematic review of studies of *E. coli* in livestock + humans

45 studies met inclusion criteria

Too heterogeneous for meta-analysis

Key result: only 8 of 45 concluded they had evidence of animal to human transfer



Muloi *et al*. (in press) *FBPD*

BACTERIA IN HUMANS AND LIVESTOCK

ST5 IN HUMANS + POULTRY

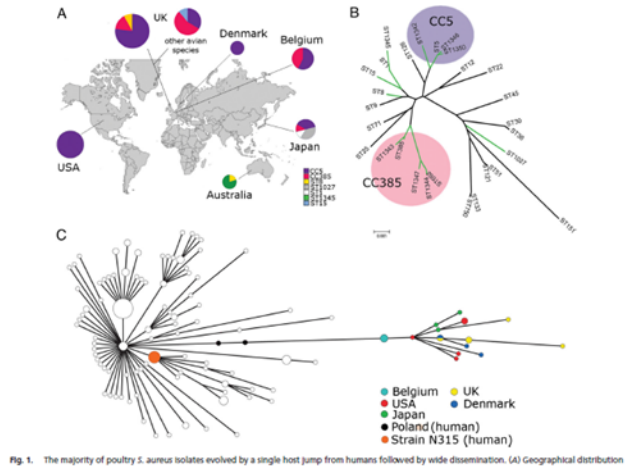
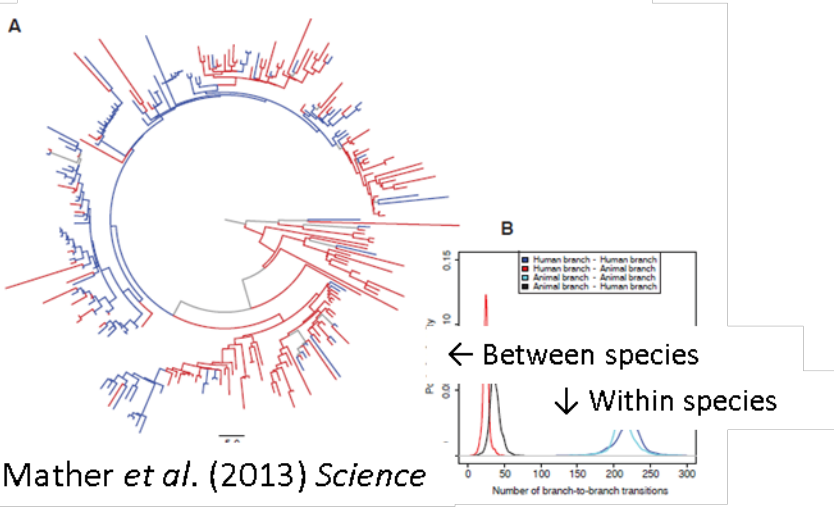


Fig. 1. The majority of poultry *S. aureus* isolates evolved by a single host jump from humans followed by wide dissemination. (*A*) Geographical distribution

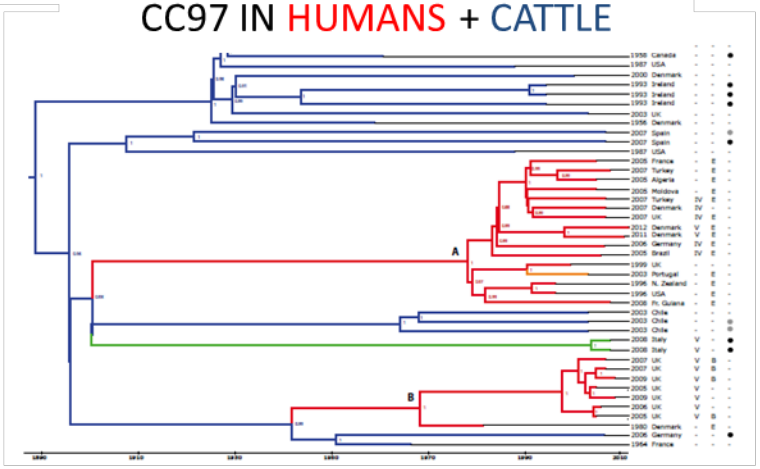
Lowder *et al.* (2009) *PNAS*

DT104 IN HUMANS + CATTLE



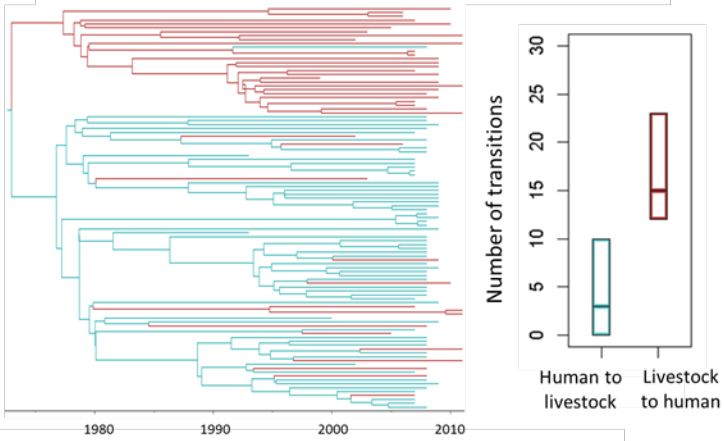
Mather *et al.* (2013) *Science*

CC97 IN HUMANS + CATTLE



Spoor *et al.* (2013) *mBio*

CC398 IN HUMANS + LIVESTOCK

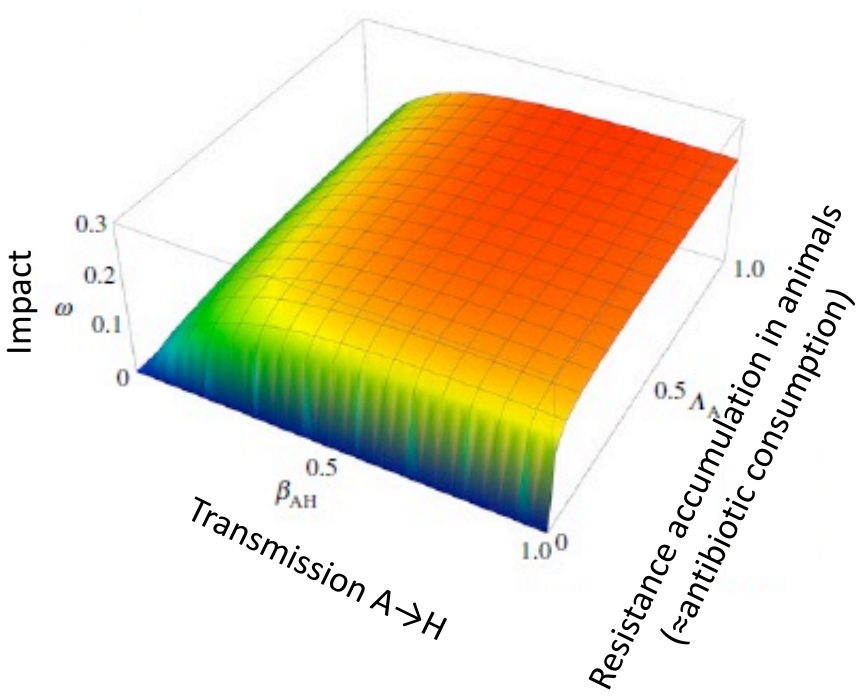


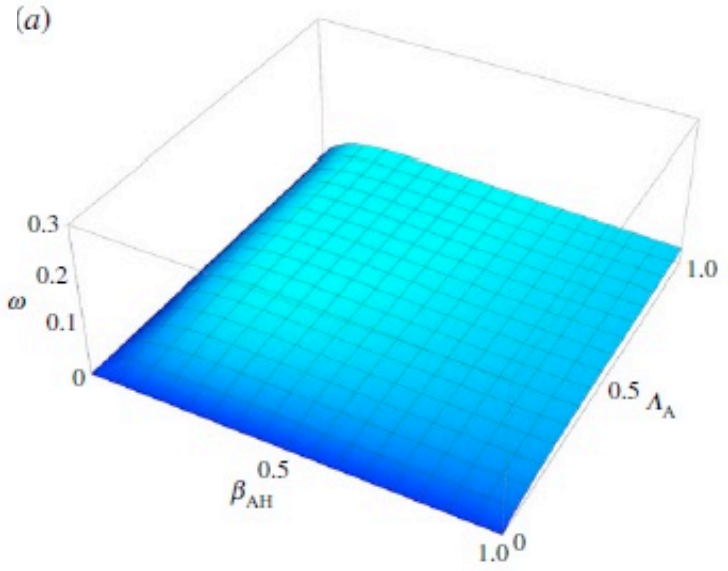
Ward *et al.* (2014) *AEM*

TWO-WAY TRAFFIC

Low transmission H→A

High transmission H→A



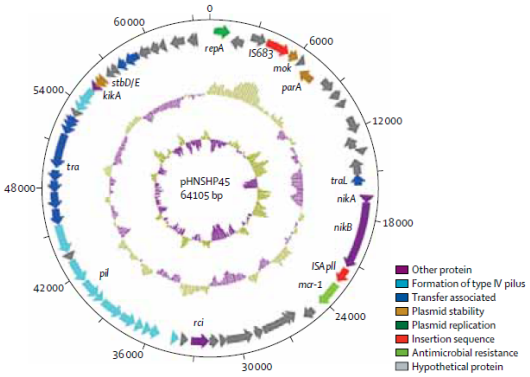


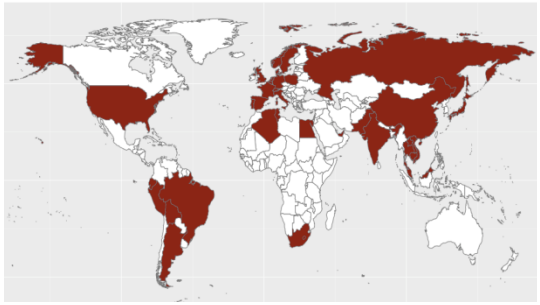
- Keep new antibiotics for human use only (Smith *et al.* 2002 *PNAS*)
- For widely used antibiotics with established resistance, stand-alone measures not very effective
- **Need integrated approach**

van Bunnik & Woolhouse (2017) *RS Open Sci*

COLISTIN RESISTANCE

- Polymyxin class antibiotic discovered in 1949
- Widely used in agriculture (esp. China) but little used in humans due to nephro- and neuro-toxicity
- New plasmid-mediated colistin resistance gene (*mcr-1*) identified in China in 2015 Liu *et al*. 2016 *LID*
- High prevalence of *mcr-1* in *E. coli* isolates from food animals and retail meat + some human patients
- Soon reported worldwide, in multiple gram –ve organisms and from many different sources
- Oldest positive isolates may date back to 1980's (chickens in China) Shen *et al*. 2016 *LID*
- Since found *mcr-2*, *3*, *4* and *5*





Failure of global surveillance?

REDUCING ANIMAL USAGE

Global Solutions:

- Reduce meat consumption
- User fees
- 50% levy at point of manufacture or wholesale importation
- Regulation
- limit usage to 50 mg/kg
- phase out growth promoters

POLICY FORUM

GLOBAL HEALTH

Achieving global targets for antimicrobial resistance

The UN should promote targets, funding, and governance

By **Ramanan Laxminarayan,[1] Devi Sridhar,[2] Martin Blaser,[3] Minggui Wang,[4] Mark Woolhouse[2]***

After decades of neglect, antimicrobial resistance (AMR) has captured the attention and concern of the public health community and global leaders. In September 2016, a high-level meeting of the United Nations General As-

We propose that no country consume more than the current median global level [8.54 defined daily doses (DDDs) per capita per year] (see the figure). We estimate that this would lower overall human use by 17.5% globally [see (*3*); see supplementary materials (SM)]. Reducing use is accomplished by improving public health and sanitation. In low-income countries, antibiotics are used to compensate for the lack of public health infrastruc-

POLICY FORUM

GLOBAL HEALTH

Reducing antimicrobial use in food animals

Consider user fees and regulatory caps on veterinary use

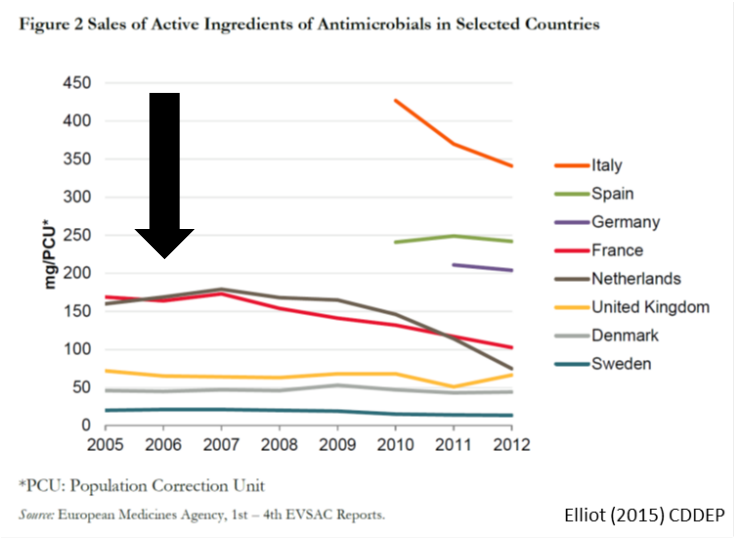
By **Thomas P. Van Boeckel,[1] Emma E. Glennon,[2,3] Dora Chen,[2,4] Marius Gilbert,[5,6] Timothy P. Robinson,[7,8] Bryan T Grenfell,[4,9] Simon A. Levin,[4,10] Sebastian Bonhoeffer,[1] Ramanan Laxminarayan[2,10]**

tin (*3*), is an important challenge for human medicine because it can lead to untreatable infections. Evidence linking AMR between animals and humans is particularly strong for common foodborne pathogens resistant to quinolones, such as *Campylobacter*

this measure could have an indirect but substantial impact on the global consumption of veterinary antimicrobials. A third solution to cut antimicrobial use would be to charge a user fee, paid by veterinary drug users, on sales of antimicrobials for nonhuman use

ANTIBIOTICS ON THE FARM

- EU growth promoter ban 2006
- European Surveillance of Veterinary Antimicrobial Consumption (ESVAC)



- Increased therapeutic and metaphylactic use
- Increased prophylactic use (especially poultry)
- Little impact on resistance in humans

2016 UN RESOLUTION

HIGH-LEVEL MEETING ON ANTIMICROBIAL RESISTANCE

21 SEPTEMBER 2016, UN HEADQUARTERS, NEW YORK

WORDS → ACTIONS → CHANGE

Mark Woolhouse, University of Edinburgh, April 2018

ACKNOWLEDGEMENTS

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- Stefan Rooke
- Devi Sridhar
- Nick Sparks (SRUC)
- Minggui Wang (Fudan Univ.)
- Melissa Ward
- Catriona Waugh
- Shengyuan Zhao

wellcome trust

EvoTAR
Evolution and Transfer of Antibiotic Resistance

SIRN

compare

Health Protection Scotland

NHS National Services Scotland

SEVENTH FRAMEWORK PROGRAMME

MRC Medical Research Council

jpiamr Joint Programming Initiative on Antimicrobial Resistance