Swiss Re Institute

Welcome and introduction

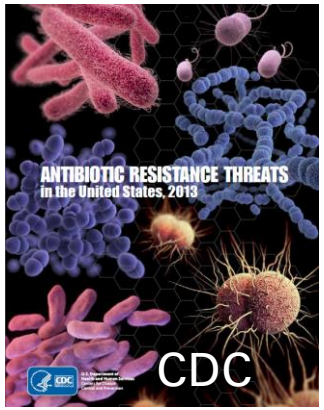
Urs Widmer, Medical Officer, Swiss Re

Antibiotic Resistance is now a global threat

E. faecium
S. aureus – Methicillin
K. pneumoniae – 3rd gen cephalosporins, carbapenems
A. Baumann – Multidrug resistant (MDR) (XDR)
P. aeruginosa
Enterobacter species - (MDR)
S. pneumoniae – Penicillin
Salmonella – Fluoroquinoles
Shigella – Fluoroquinoles
N. gonorrhea – 3rd gen. cephalosporins
E. coli – 3rd gen. cephalosporins, fluoroquinolines

ESKAPE are the leading causes of hospital acquired infections throughout the world

XDR typhoid in Pakistan carries added resistance genes

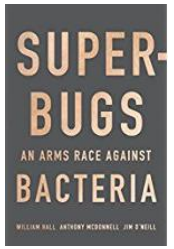


We need to develop novel antibiotics and alternatives to conventional antibiotics

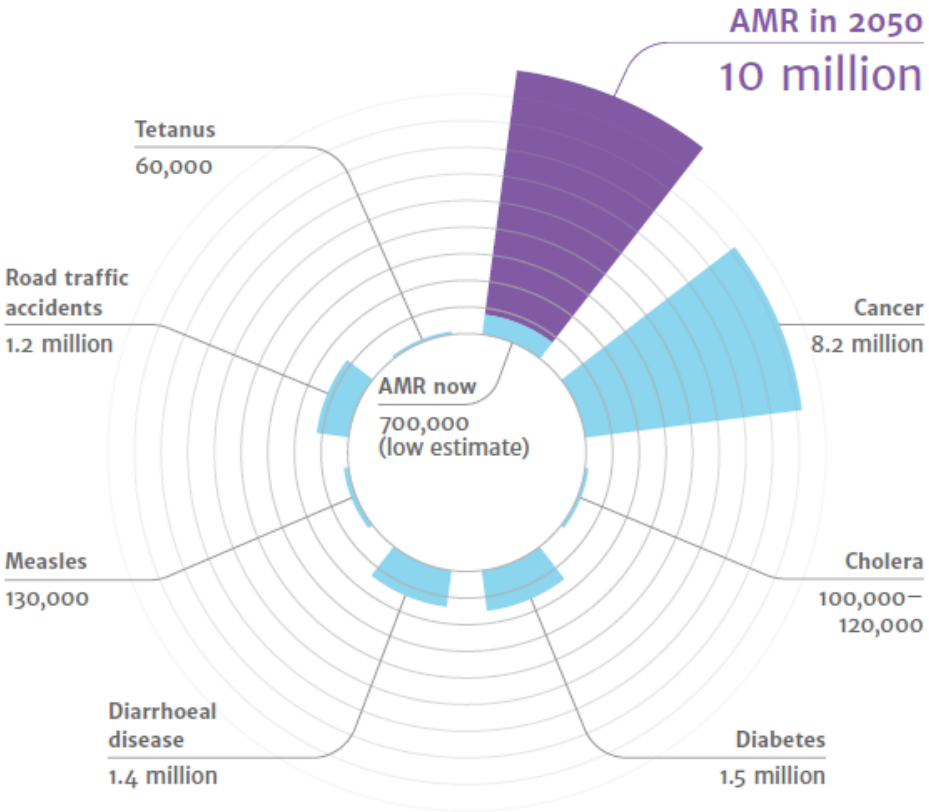
Antimicrobial Resistance

Tackling a crisis for the health and wealth of nations

Chaired by Jim O'Neill, December 2014

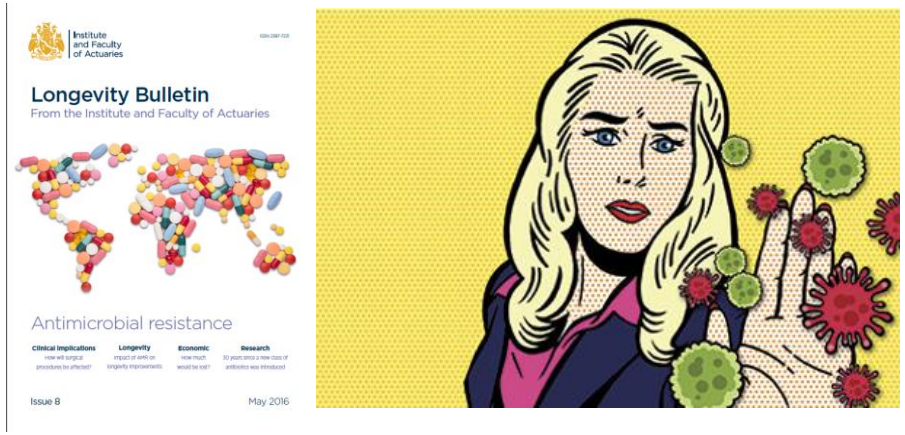


Deaths attributed to AMR every year compared to other major causes of death

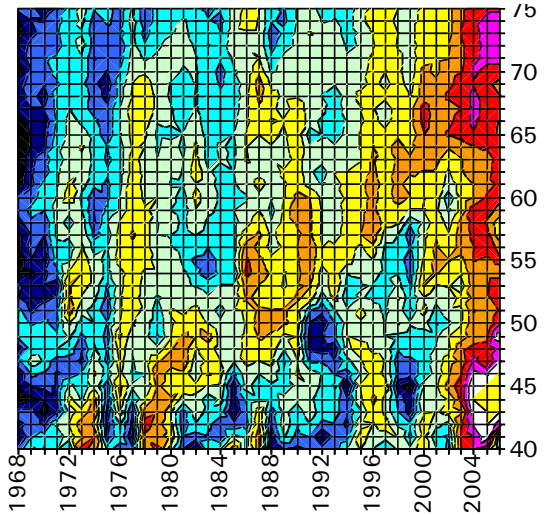


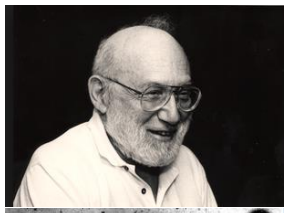
AMR's impact on World GDP in trillions of USD

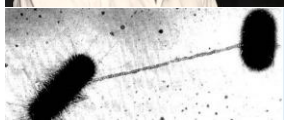
TheActuary
The magazine of the Institute & Faculty of Actuaries



Plausible mortality improvements vs. mortality deterioration from AMR

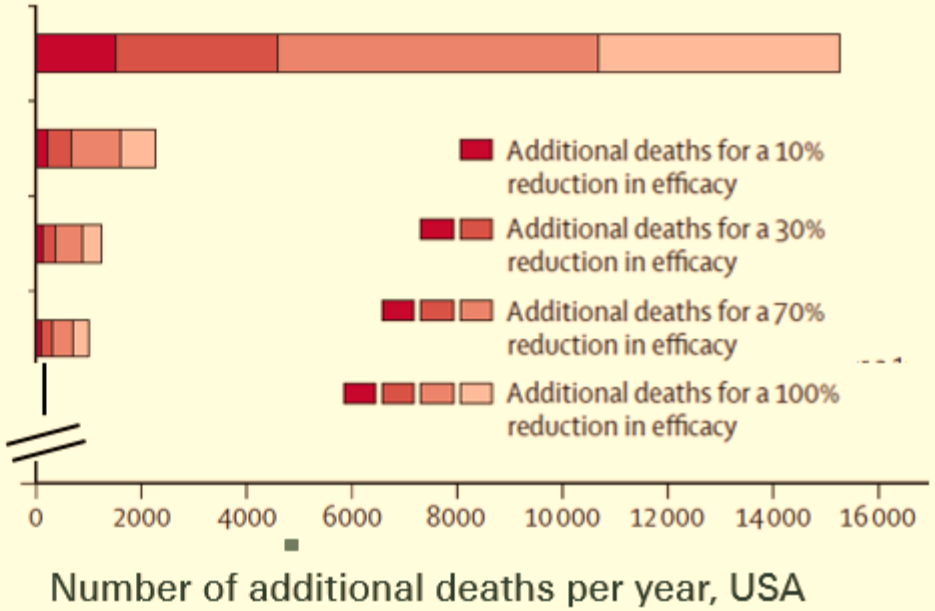






Burden of AMR on antibiotic prophylaxis for surgery and cancer chemotherapy

- Colorectal surg.
- Cancer chemoth.
- Total hip repl.
- Prostate biopsy



Teillant et al. Lancet Infect Dis 2015; 15: 1429–37

P&C Claims due to AMR –a costing topic, but not an accumulation issue

Ballad of *Typhoid Mary* in the era of Next Generation Sequencing (NGS)

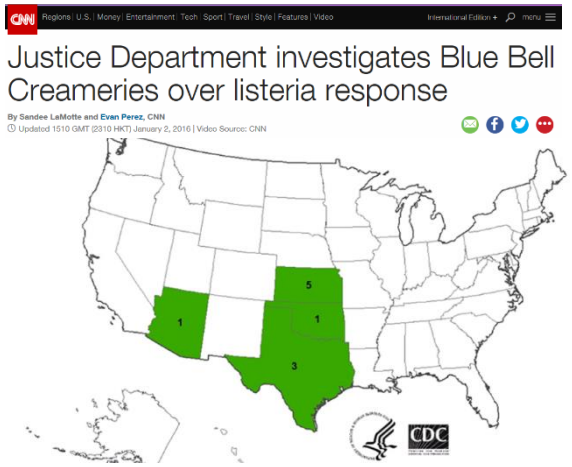
1. Health Technology Hazard - Endoscopy-associated deadly infections with resistant bacteria

3. Contamination of live-stock

4. Medical Malpractice

5. Business Interruption ICU, Hospital Ward

2. Foodborne-disease outbreaks



PulseNet USA
www.cdc.gov/pulsenet)

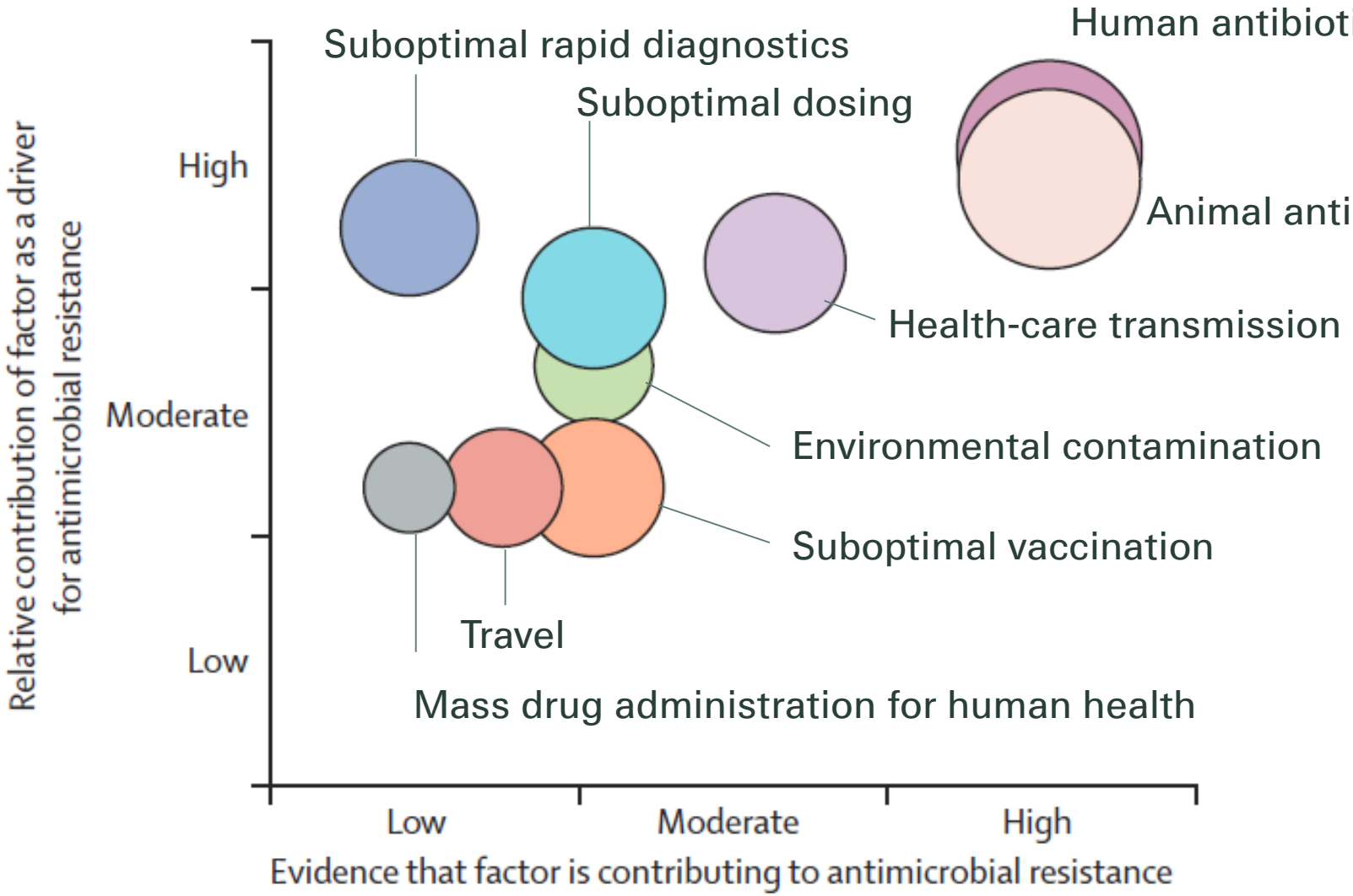
Food companies:

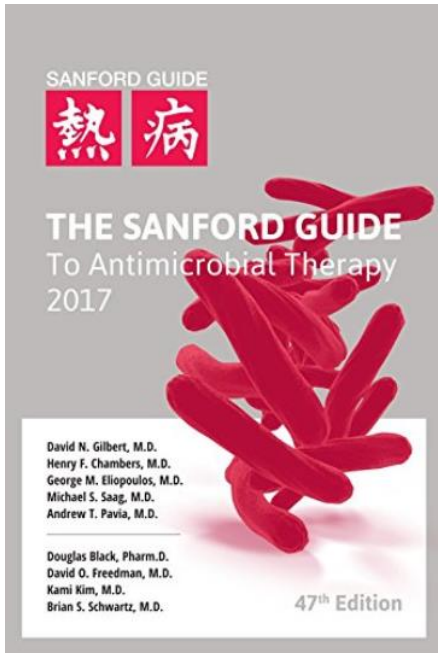
- WGS: More outbreaks discovered
- More recalls?
- Expect more lawsuits?
- Face more criminal charges?

Insurers:
Claims series clause, Claims trigger
Retroactive date, Status of limitation

Source: Modified from juerg.a.schmid@zurich.com

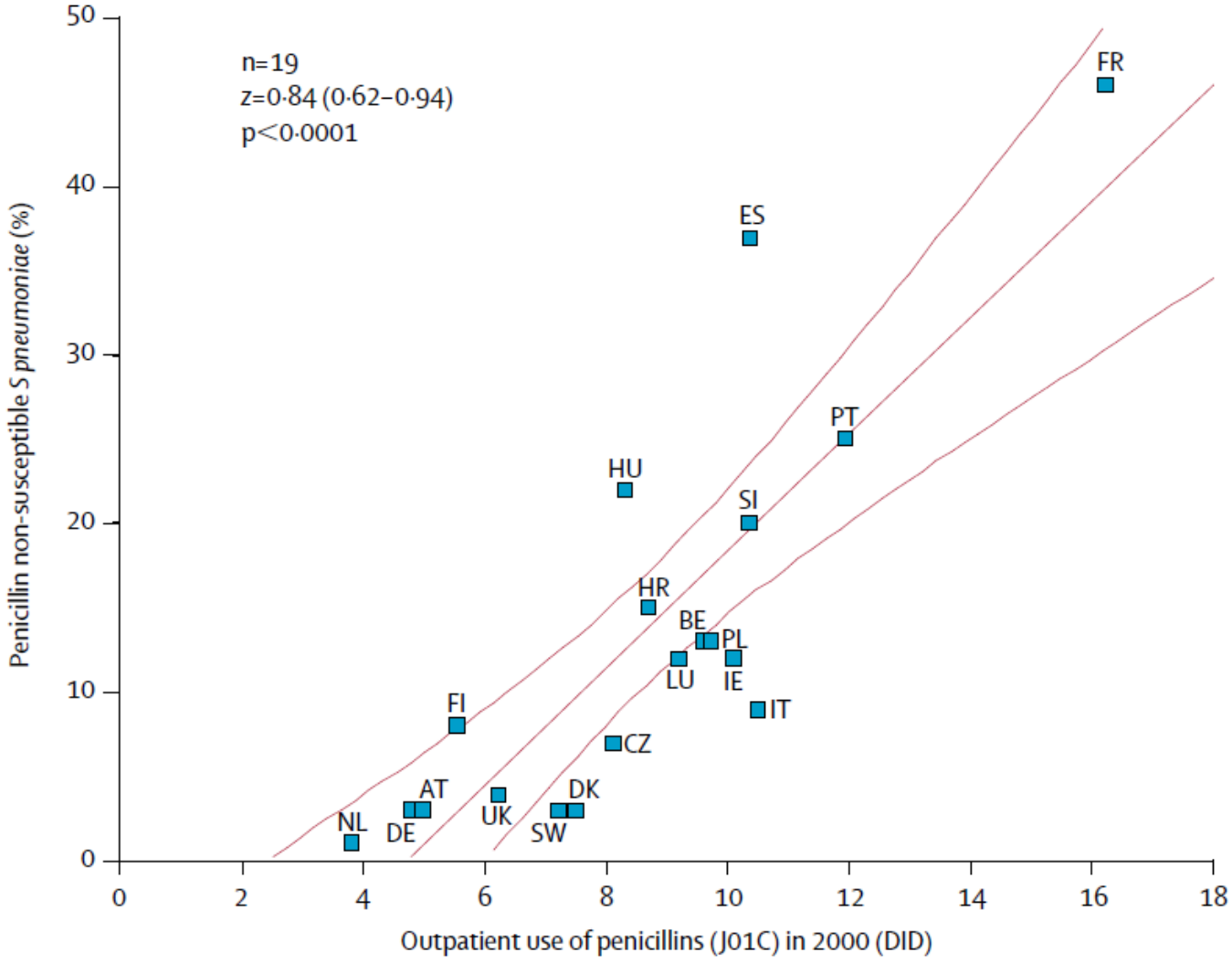
Discussed Drivers of AMR



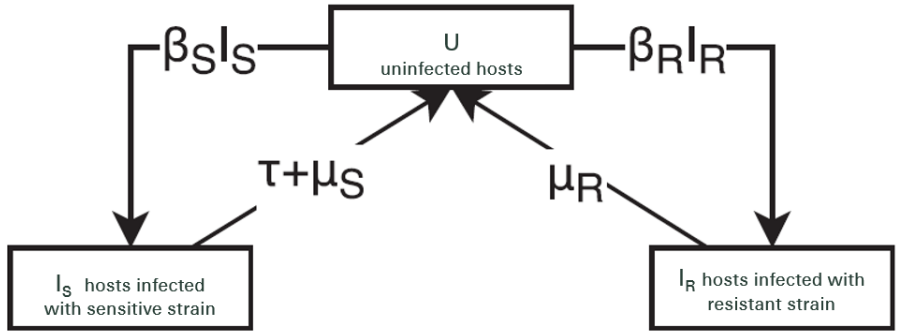


Lancet 2016; 387: 176–87

More Abx use = more resistance



Goossens H. et al. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. Lancet 2005; 365: 579–87



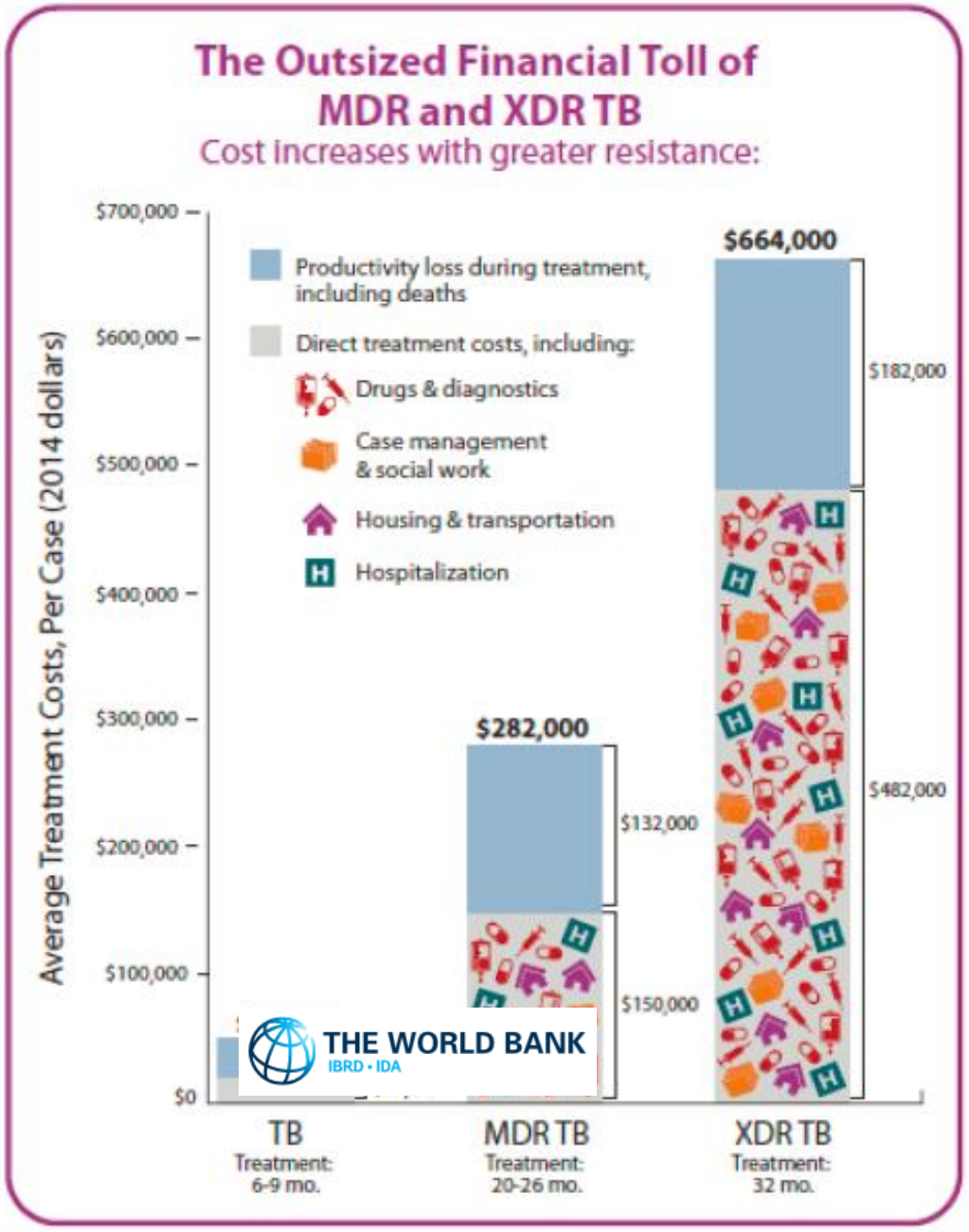
Antibiotic **resistant** and **sensitive** strains compete for available hosts— we would therefore expect the fitter strain to dominate. Instead, we observe **stable coexistence** of both strains.

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH

Marc Lipsitch

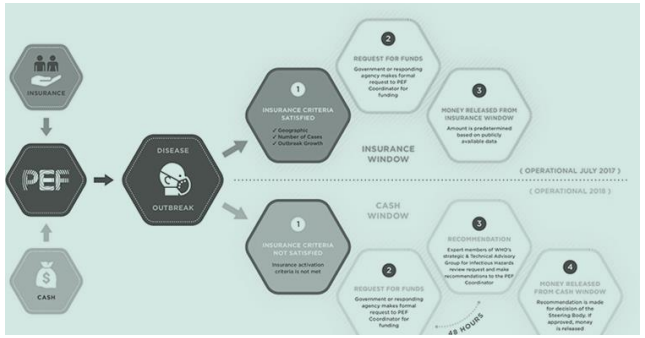
Professor of Epidemiology

Lehtinen et al. Proc Natl Acad Sci U S A. 2017 Jan 31;114(5):1075-1080



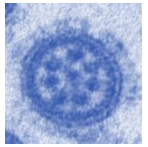
US Secretary of State Hillary Rodham Clinton, Dartmouth College President Jim Yong Kim, and US Secretary of the Treasury Timothy F. Geithner listen while US President Barack Obama speaks in the Rose Garden of the White House on March 23, 2012 in Washington, DC. President Obama announced his nomination of Kim to succeed Robert Zoellick as President of the World Bank.

PANDEMIC EMERGENCY FINANCING FACILITY

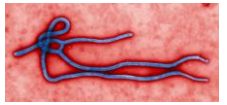


THE WORLD BANK
Swiss Re
Munich RE
AIR
WHO

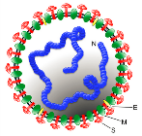
Influenza



Filovirus



Coronavirus



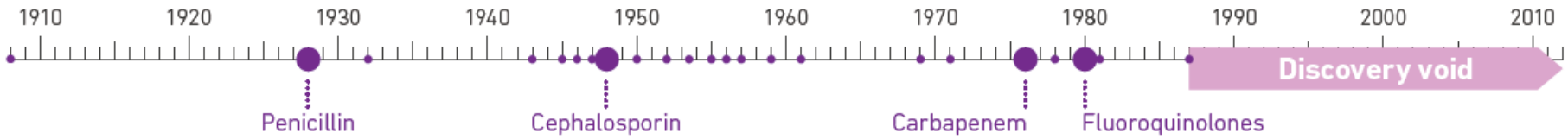
Various

- Crimean-Congo Fever
- Rift Valley
- Lassa Fever

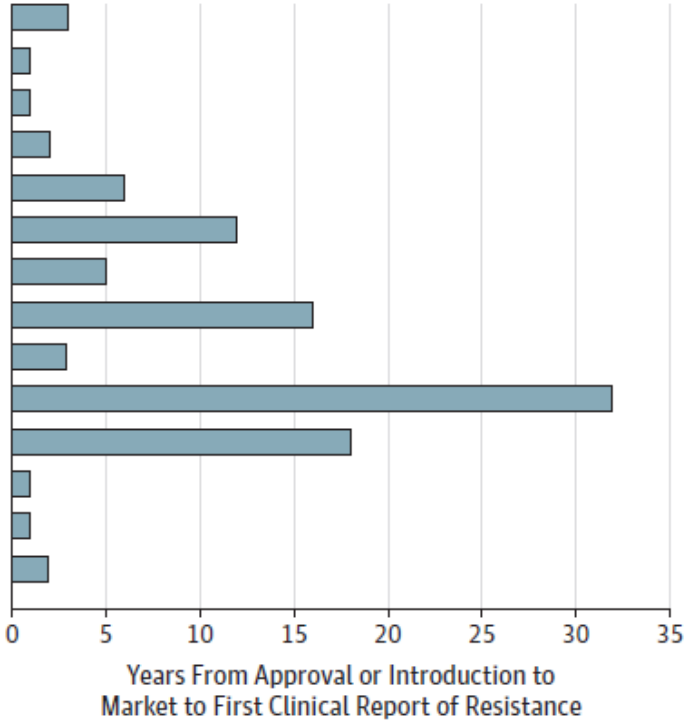
©CDC, TB fact sheet, 2015

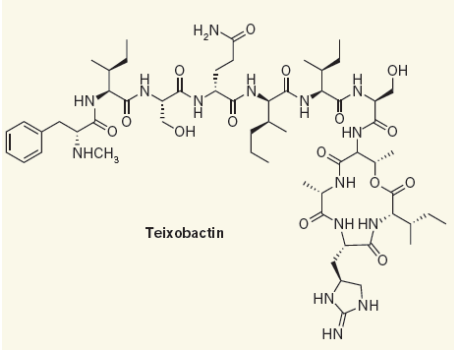
The Void

Over the last 30 years, no major new types of antibiotics have been developed



Class	Antibiotic	Year of Approval or Introduction to Market
β-Lactams	Penicillin	1942
	Methicillin	1960
	Cephalothin	1964
	Amoxicillin-clavulanic acid	1984
Carbapenems	Imipenem-cilastatin	1985
Amphenicols	Chloramphenicol	1950
Tetracyclines	Tetracycline	1953
Aminoglycosides	Streptomycin	1946
Macrolides	Erythromycin	1952
Glycopeptides	Vancomycin	1958
Quinolones	Nalidixic acid	1964
Streptogramins	Quinupristin-dalfopristin	1999
Oxazolidinones	Linezolid	2000
Lipopeptides	Daptomycin	2003





Teixobactin

Τεἰχος (engl. «the wall»)

nature microbiology — LETTERS
https://doi.org/10.1038/s41564-018-0110-1
OPEN

Culture-independent discovery of the malacidins as calcium-dependent antibiotics with activity against multidrug-resistant Gram-positive pathogens

LETTER
doi:10.1038/nature26157

A new class of synthetic retinoid antibiotics effective against bacterial persisters

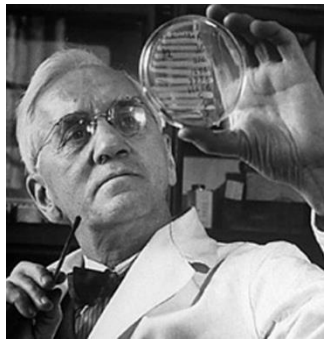
Wooseong Kim[1], Wenpeng Zhu[2], Gabriel Lambert Hendricks[1], Daria Van Tyne[3,4], Andrew D. Steele[5,6], Colleen E. Keohane[5,6], Nico Fricke[2], Annie L. Conery[7,8], Steven Shen[1], Wen Pan[1], Kiho Lee[1], Rajmohan Rajamuthiah[1], Beth Burgwyn Fuchs[1], Petia M. Vlahovska[9], William M. Wuest[5,6], Michael S. Gilmore[3,4], Huajian Gao[2], Frederick M. Ausubel[7,8] & Eleftherios Mylonakis[1]

Strategies to find natural products with antimicrobial properties

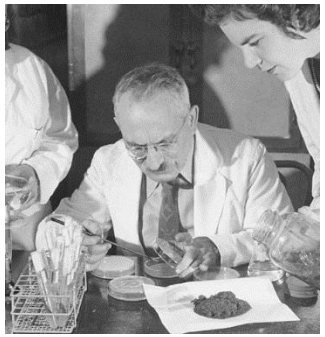
Culture-dependent discovery

Metagenomics

Culture-independent discovery



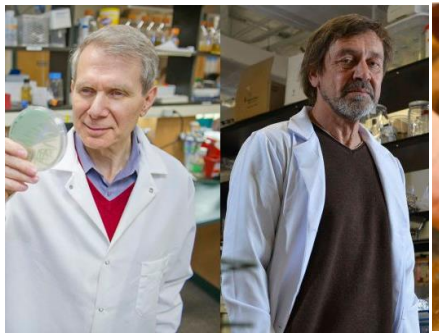
Alexander Fleming



Selman A. Waksman

Next generation soil people

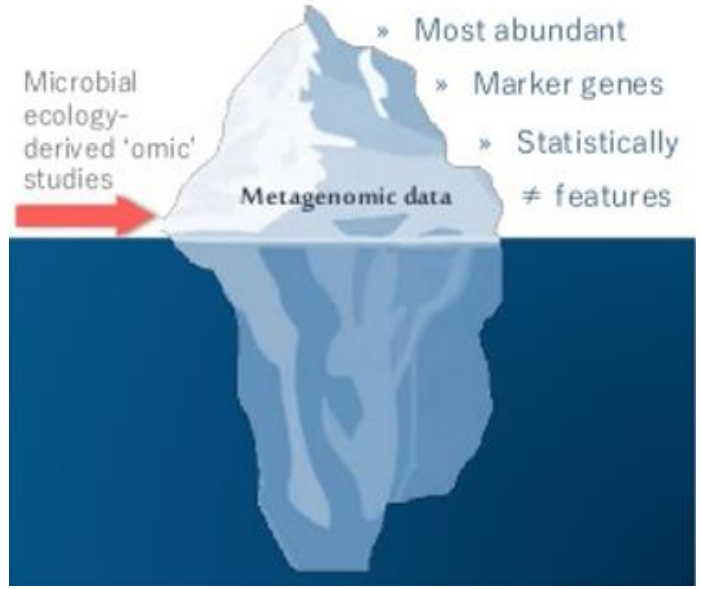
iChip (i=isolation) is a new trick for culture



Kim Lewis & s.epstein@northeastern.edu with iChip

Enrichement and eDNA extraction

- Microorganisms largest proportion of biomass on Earth,
- inhabiting variety of ecosystems, including hot springs, salt brines, acid mine waters at pH near zero, Antarctic ices
- Environmental DNA (eDNA) analysis of microbial communities estimates that only 0.1% to 1% of these prokaryotes are culturable



JAMA. 2016;316(11):1193-1204

doi:10.1038/nrd.2018.36

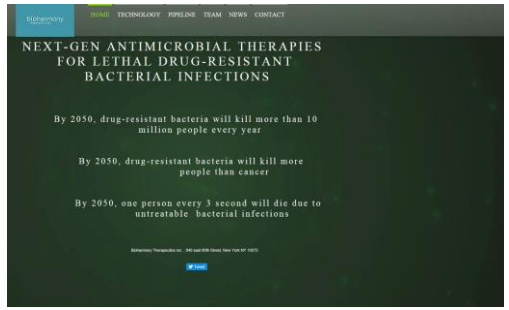
Valuation

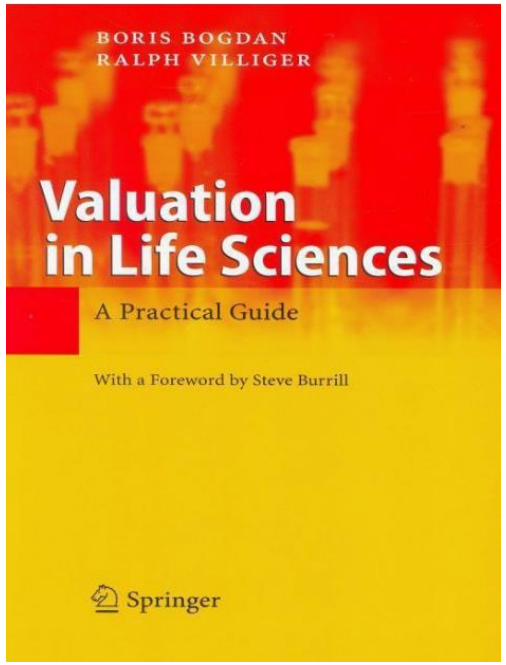
1 *iChip*

2 *Lysins Gram+*

3 *Lysins Gram-*

Company	Novobiotic	ContraFect NASDAQ: CFRX	Bioharmony Therpeutics Inc
Pipeline	Teixobactin	CF-301 (exebacase) Gram-negative lysins	Gram-negative lysins For Burns
Source & Strategy	Eleftheria terrae (Gram-neg) iCHIP	Recombinant bacteriophage-derived lysin	
Mechanism of action	Inhibits cell wall growth	lysis	
Bacteria Class	Tuberculosis MRSA Vancomycin-res. Enterococci VRE	Methocillin resistant strains Biofilm Gram pos	Pseudomonas aeruginosa Gram neg
Development Stage	Praeclinic	Clinical Phase II, multi-center study	
Financing	Private Company, Grants (NIH) & Foundation (Gates)	Stock Company	Private Company
Chief scientific advisory	Kim Lewis, Ph.D., Co-founder Slava Epstein, Ph.D., Co-founder	Vincent A. Fischetti, Ph.D. Scientific Advisory Board	Vincent A. Fischetti, Ph.D. Scientific Advisory Board

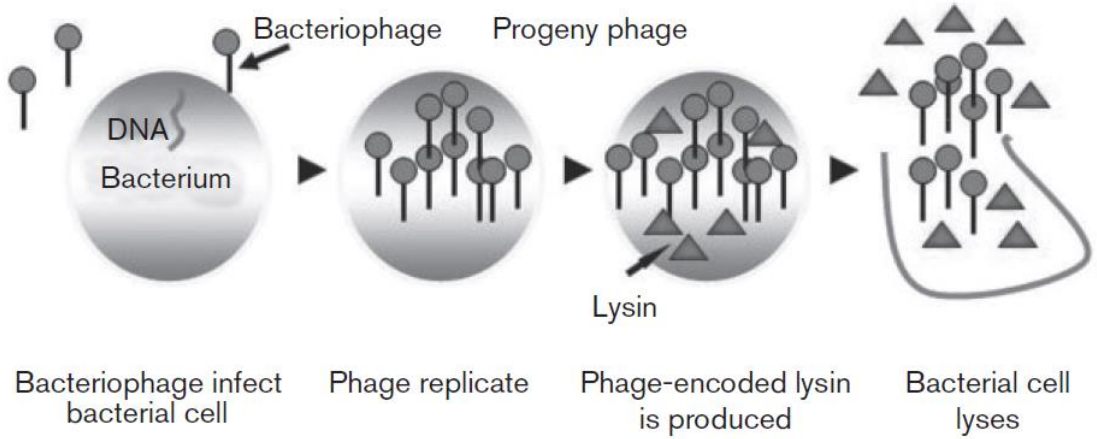


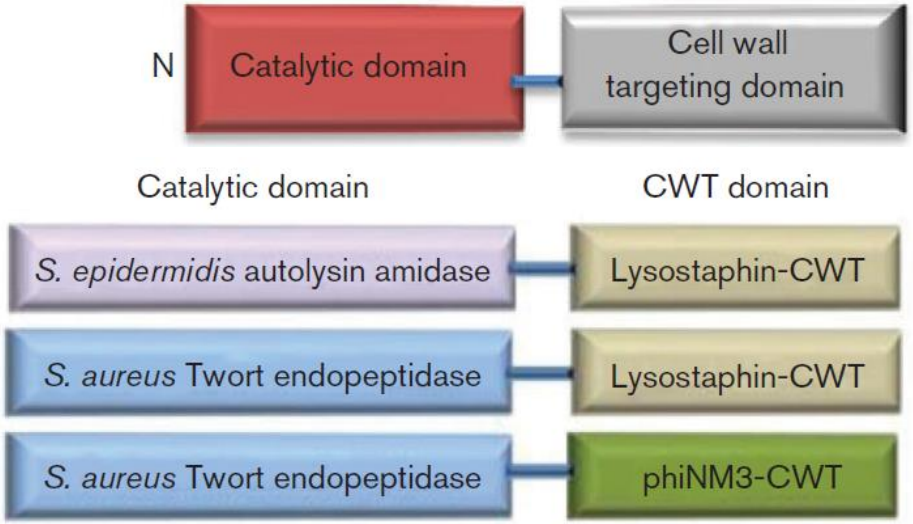


Boris Bogdan and Ralph Villiger
ISBN-13: 978-3642108198

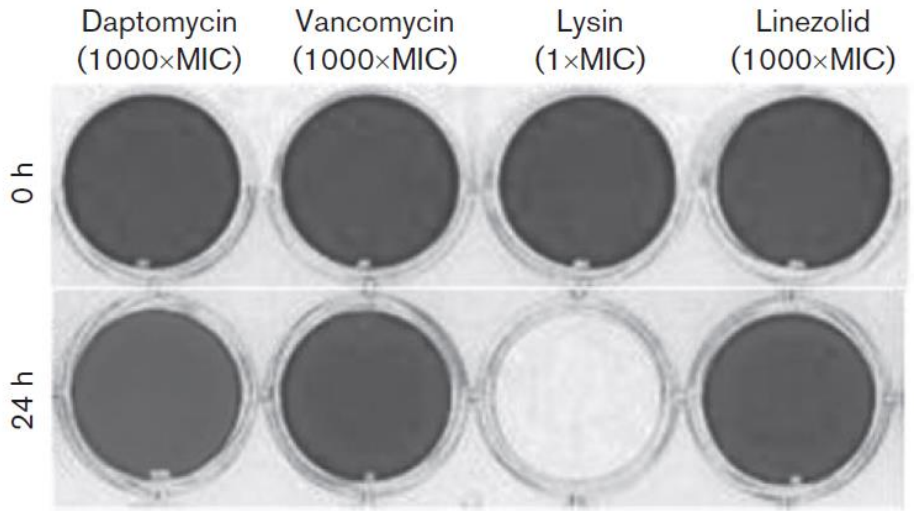
New Arrival

Lysins: Pathogen-directed anti-infectives





Biofilm assay (*S aureus*)



Kathy Kroll
ZHAW

Michael Altorfer
Swiss Biotech Association

Marie Petit
Biotech companies in EU combating AMR

Peter Beyer
WHO

Christoph Spennemann
UN Conference on Trade and Development

Swiss Re

Life & Health
Yommy Chiu
Richard Francis
Manuel Villegas Caballero
Urs Widmer

Property & Casualty
Ramiro Dip
Rainer Egloff
Bernd Wilke
Petra Winter

ZURICH

Jürg Schmid
Jelena Buha

Academia

Jennifer Rohn
University College London

Stephan Harbarth
HUG

Thomas von Boeckel
ETH

Cedric Müntener
Zurich University

Roger Kouyos
USZ, Zurich University


https://demystifyingmedicine.od.nih.gov

Drivers of antimicrobial resistance

1.	Global trends in antimicrobial use in food animals	Thomas van Boeckel
2.	Use of Antibiotics in Livestock and Human Health Concerns	Cedric Müntener
3.	Identifying the drivers of antimicrobial resistance	Roger Kouyos

WS 1a - AMR surveillance strategies – Magnitude of global threat and expected mortality or liability claims *(Repeat 1x)*

WS 2a - Using antibiotics wisely in a One Health world – how can insurance incentivize? *(Repeat 1x)*

WS 3a - Modelling AMR, what is a reinsurer's mortality exposure? *(Repeat 1x)*

Preventing the "Post-Antibiotic Apocalypse"

1.	Strategies to battle AMR - New funding mechanisms and paradigm shifts	Marie Petit
2.	Case study: Murepavadin is a new antibiotic class in the pipeline	Michael Altorfer
3.	How to reinvigorate the current R&D pipeline	Peter Beyer
4.	Fostering investment in AMR innovation	Christoph Spennemann

WS 4: Cost Sharing in Insurance Coverage for antibiotic-resistant infections, an example of Precision Medicine

WS 5: Alternative business model options for antibiotics development – ideas from insurers?

WS 6: Scientific innovation in antibiotic drug discovery - Examples of new platforms and novel compounds

Panel Discussion

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Agenda

13.20 **Welcome and introduction**
Urs Widmer, Medical Officer, Swiss Re

13.30 **Global trends in antimicrobial use in food animal**
Thomas van Boeckel, Theoretical Biology, ETH Zurich

13.45 **Use of Antibiotics in Livestock and Human Health Concerns**
Cedric Müntener, Institute of Veterinary Pharmacology and Toxicology, University of Zurich

14.00 **Identifying the drivers of antimicrobial resistance**
Roger Kouyos, Department of Infectious Diseases, University of Zurich

Swiss Re Institute

Global trends in antimicrobial use in food animals

Thomas van Boeckel, Theoretical Biology, ETH Zurich

Swiss Re Institute

Use of Antibiotics in Livestock and Human Health Concerns

Cedric Müntener, Institute of Veterinary Pharmacology and Toxicology, University of Zurich

Swiss Re Institute

Identifying the drivers of antimicrobial resistance

Roger Kouyos, Department of Infectious Diseases, University of Zurich

Swiss Re Institute

14.15 **Workshop Series I**

Session 1: *Forum B*
AMR surveillance strategies – Magnitude of global threat and expected mortality or liability claims

Experts: Stephan Harbarth, Jennifer Rohn
Moderators: Jürg A. Schmid, Urs Widmer

Session 2: *Library*
Using antibiotics wisely in a One Health world – how can insurance incentivize?

Experts: Thomas van Boeckel, Cedric Müntener
Moderators: Ramiro Dip

Session 3: *Seminar Room 4*
Modelling AMR, what is a reinsurer's mortality exposure?

Experts: Roger Kouyos
Moderators: Yommy Chiu, Manuel Villegas Caballero

Swiss Re Institute

15.15 **Coffe break**

15.30 **Strategies to battle AMR - New funding mechanisms and paradigm shifts**
Marie Petit, BEAM Alliance

15.40 **Case study: Murepavadin is a new antibiotic class in the pipeline to treat resistant Pseudomonas infections**
Michael Altorfer, CEO Swiss Biotech Association

15.50 **How to reinvigorate the current R&D pipeline**
Peter Beyer, Senior Advisor, World Health Organization (WHO)

16.00 **Fostering investment in AMR innovation**
Christoph Spennemann, Intellectual Property Unit, Division on Investment & Enterprise, UNCTAD, Geneva

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Strategies to battle AMR - New funding mechanisms and paradigm shifts

Marie Petit, BEAM Alliance

Swiss Re Institute

Case study: Murepavadin is a new antibiotic class in the pipeline to treat resistant Pseudomonas infections

Michael Altorfer, CEO Swiss Biotech Association

Swiss Re Institute

How to reinvigorate the current R&D pipeline

Peter Beyer, Senior Advisor, World Health Organization (WHO)

Swiss Re Institute

Fostering investment in AMR innovation

Christoph Spennemann, Intellectual Property Unit, Division on Investment & Enterprise, UNCTAD, Geneva

Swiss Re Institute

16.10 **Workshop Series II**

Session 4: *Library*

Cost Sharing in Insurance Coverage for antibiotic-resistant infections, an example of Precision Medicine

Experts: Michael Altorfer, Peter Beyer
Moderators: Yommy Chiu

Session 5: *Seminar Room 4*

Alternative business model options for antibiotics development – ideas from insurers?

Expert: Christoph Spennemann, Marie Petit
Moderators: Bernd Wilke

Session 6: *Forum B*

Scientific innovation in antibiotic drug discovery – Examples of new platforms and novel compounds

Expert: Jennifer Rohn, Stephan Harbarth
Moderators: Ramiro Dip, Urs Widmer

Swiss Re Institute

16.40 **Panel Discussion and Closing remarks**
Ramiro Dip and Urs Widmer

Pannelists:

- Michael Altorfer, CEO Swiss Biotech Association
- Thomas van Boeckel, Theoretical Biology, ETH Zurich
- Roger Kouyos, Department of Infectious Diseases, University of Zurich
- Cedric Müntener, Institute of Veterinary Pharmacology and Toxicology, University of Zurich
- Marie Petit, BEAM Alliance
- Christoph Spennemann, Intellectual Property Unit, Division on Investment & Enterprise, UNCTAD, Geneva
- Peter Beyer, Senior Advisor, World Health Organization (WHO)

17.15 **End of Workshop**

Swiss Re Institute

End of Workshop

See you soon for the "Risk Talks" at 17:45, same place!

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