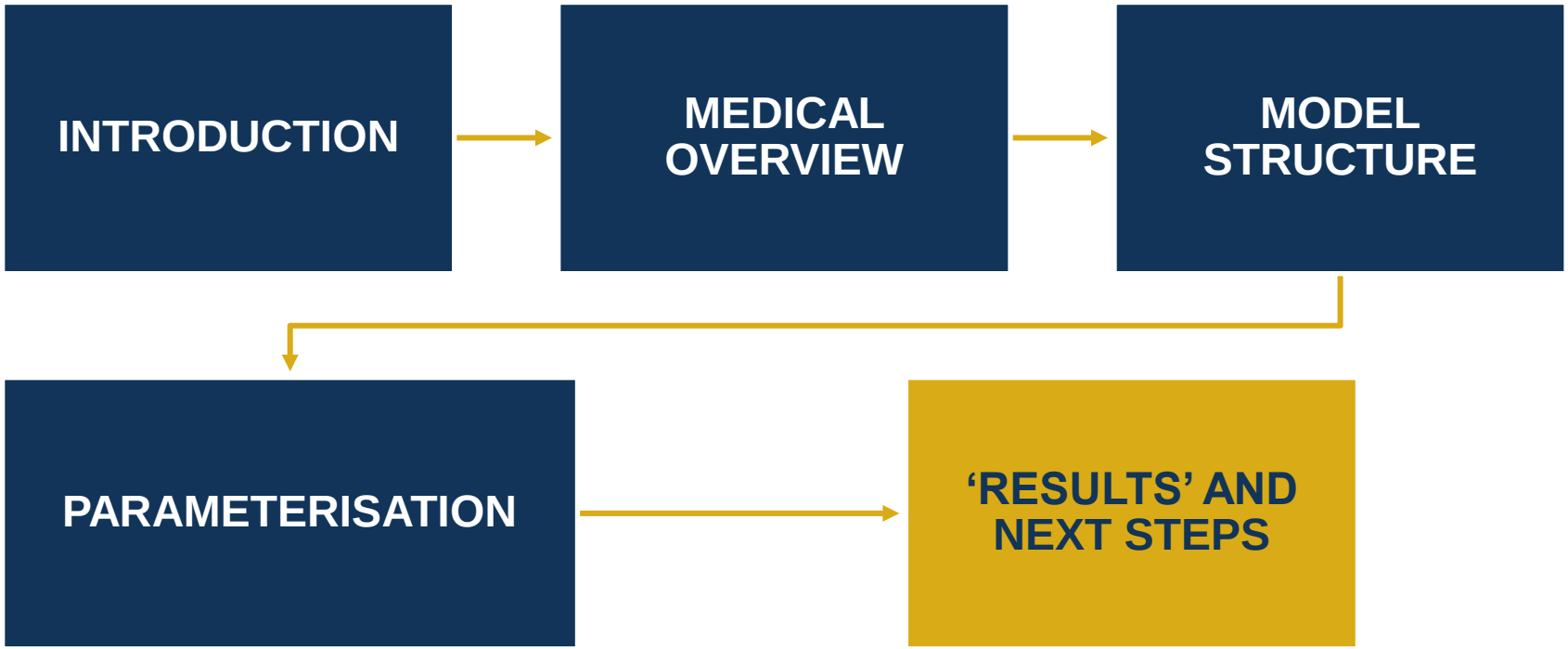
Institute and Faculty of Actuaries

When the drugs don’t work…

Nicola Oliver and Ross Hamilton
(IFoA Antibiotic Resistance Working Party)

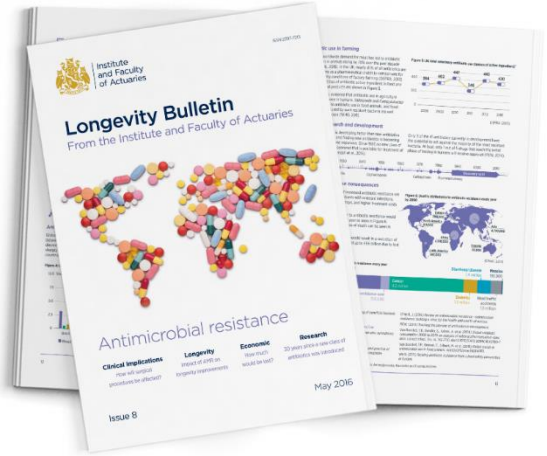
Agenda



Institute and Faculty of Actuaries

Working party background

ABR Event
Staple Inn
May 2016



- **Develop a simple modelling framework with plausible parameterisation to allow actuaries to develop their own views on likely and stress mortality impacts**
- **This framework would be developed in a UK context but would be expected to be readily transferable to other countries**
- **Working party started in January 2017**

Institute and Faculty of Actuaries

Working party members

Name	Role	Firm
Matthew Edwards	Chair	Willis Towers Watson
Nicola Oliver	Medical input & Deputy Chair	Medical Intelligence
Sheridan Fitzgibbon	Model structure & parameterisation	Legal & General
Craig Armstrong	Parameterisation (2017)	Aviva
Ross Hamilton	Model development	Lloyds Banking Group
Irene Merk	General	SCOR
Roshane Samarasekera	Model development	GAD
Soumi Sarkar	General	Legal & General
Katherine Fossett	General	Barnett Waddingham

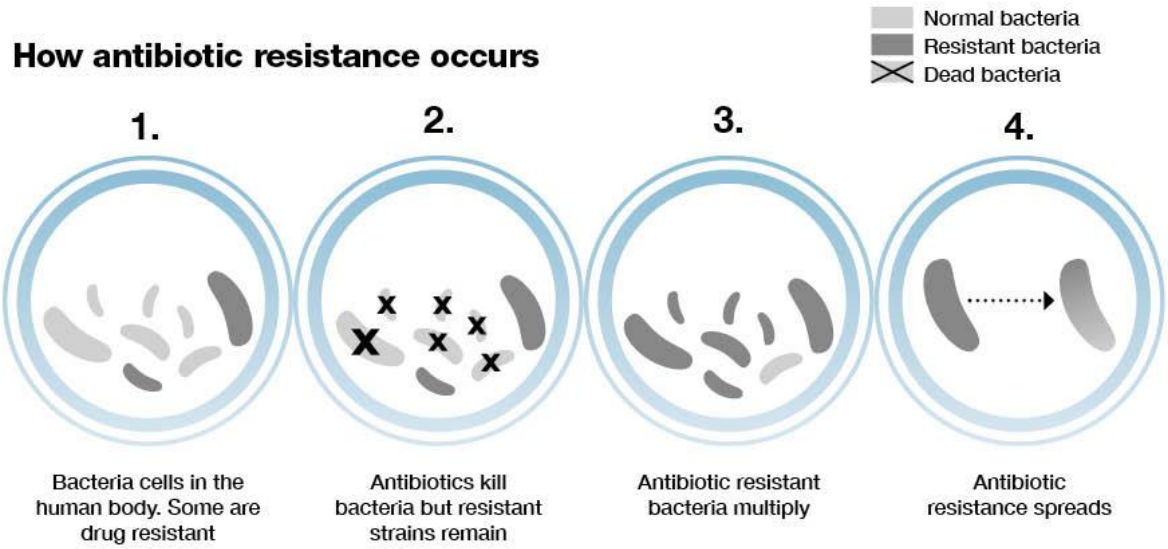
Institute and Faculty of Actuaries

Institute and Faculty of Actuaries

Medical overview

June 11, 2024

What is antibiotic resistance…

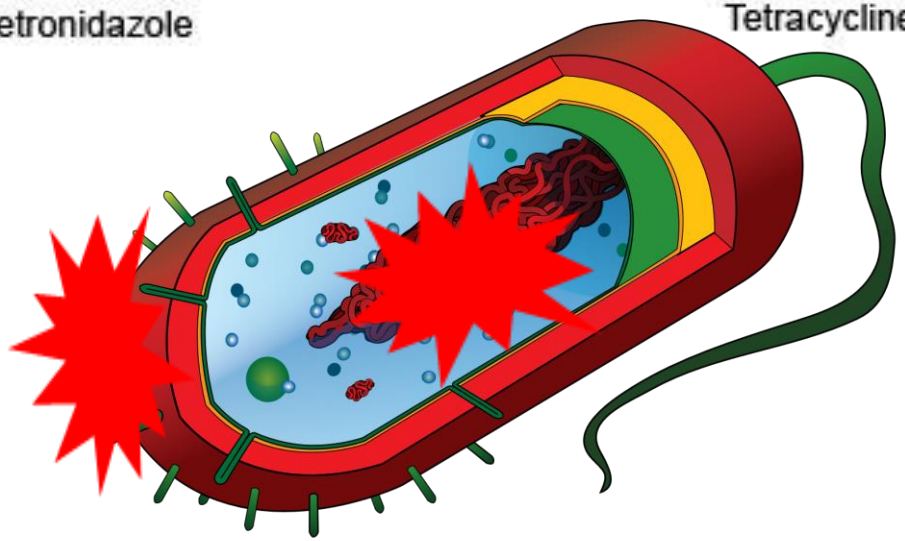


It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

"***The thoughtless person playing with penicillin treatment is morally responsible for the death of the man who succumbs to infection with the penicillin-resistant organism***." Sir Alexander Fleming, 1928

Institute and Faculty of Actuaries

EXAMPLES:
Aminoglycosides
Beta-lactams
Vancomycin
Quinolones
Rifampin
Metronidazole



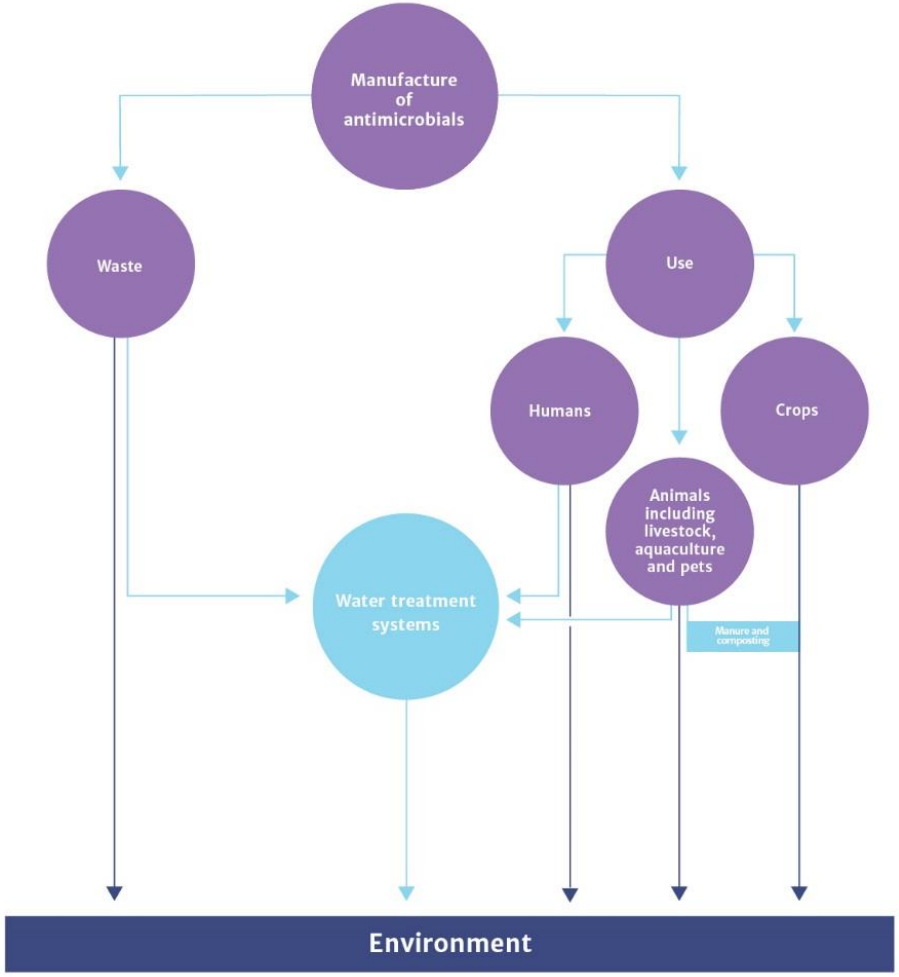
EXAMPLES:
Chloramphenicol
Erythromycin
Clindamycin
Sulfonamides
Trimethoprim
Tetracyclines

How does it actually work (the science!)

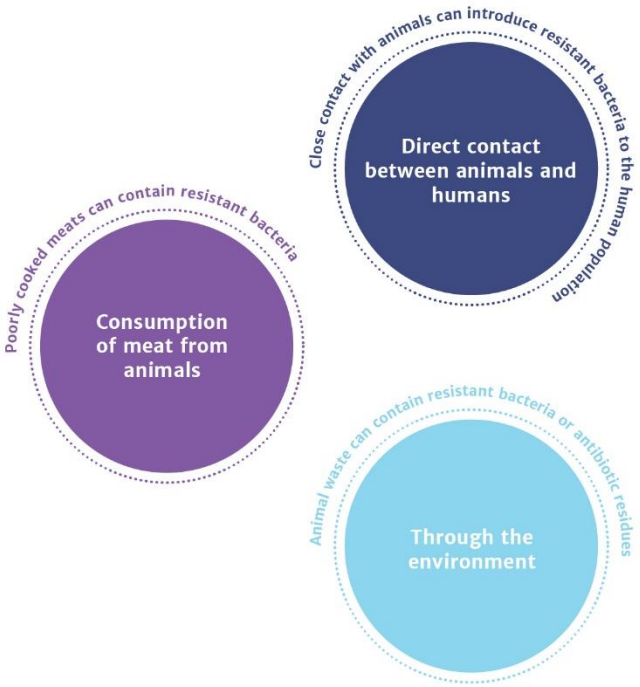
Institute and Faculty of Actuaries

What are the sources of resistance?

Sources of resistance



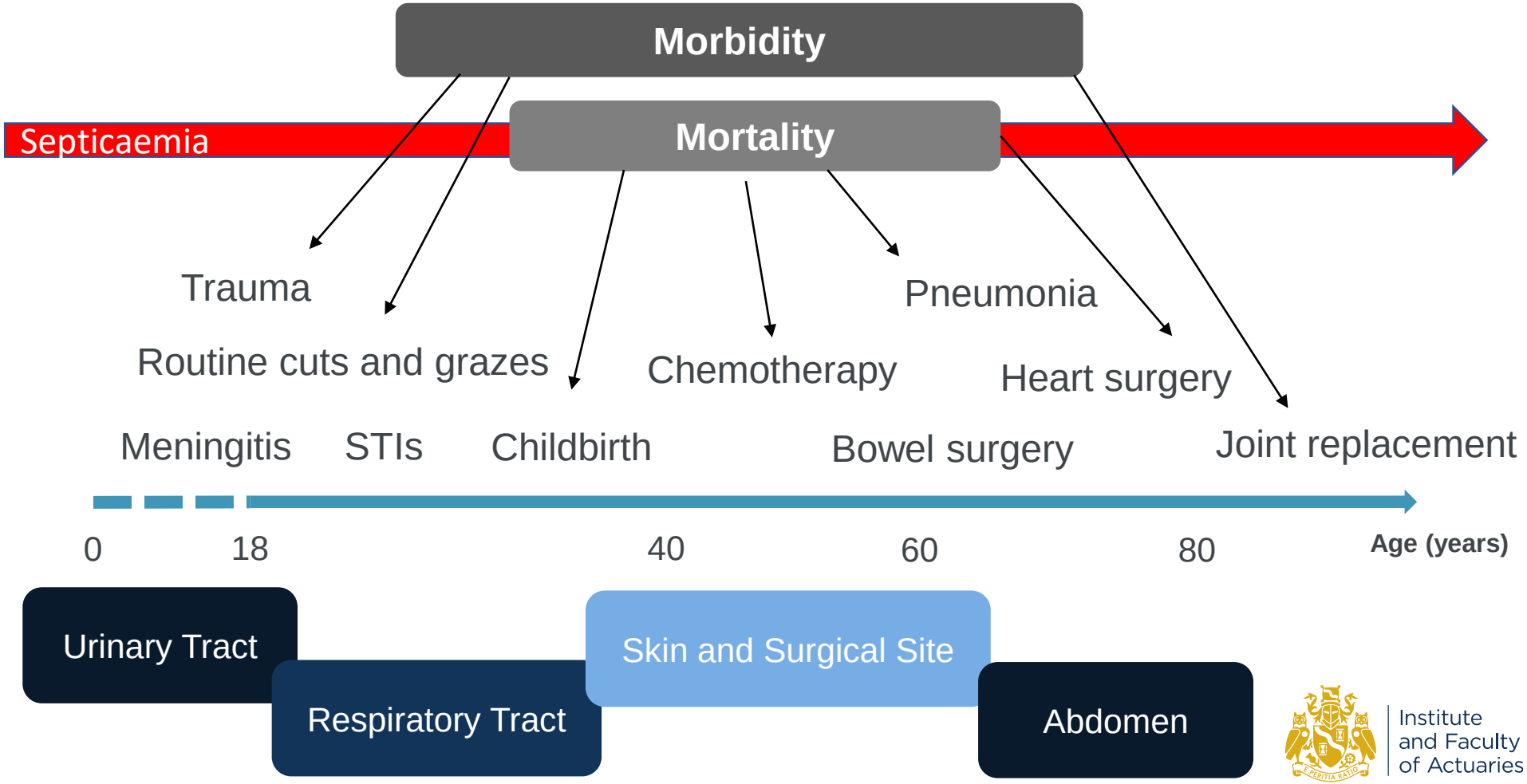
How animals can pass on resistant bacteria



Infographics sourced from "Review on Antimicrobial Resistance" 2014

Institute and Faculty of Actuaries

How does ABR affect people and our work?



Institute and Faculty of Actuaries

Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis

Evelina Tacconelli, Elena Carrara*, Alessia Savoldi*, Stephan Harbarth, Marc Mendelson, Dominique L Monnet, Céline Pulcini, Gunnar Kahlmeter, Jan Kluytmans, Yehuda Carmeli, Marc Ouellette, Kevin Outterson, Jean Patel, Marco Cavaleri, Edward M Cox, Chris R Houchens, M Lindsay Grayson, Paul Hansen, Nalini Singh, Ursula Theuretzbacher, Nicola Magrini, and the WHO Pathogens Priority List Working Group†

Criteria
Mortality
Health-care burden
Community burden
Prevalence of resistance
10-year trend of resistance
Transmissibility
Preventability in the community
Preventability in health-care setting
Treatability
Pipeline

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

Enterobacteriaceae, carbapenem-resistant, 3rd generation cephalosporin-resistant

Institute and Faculty of Actuaries

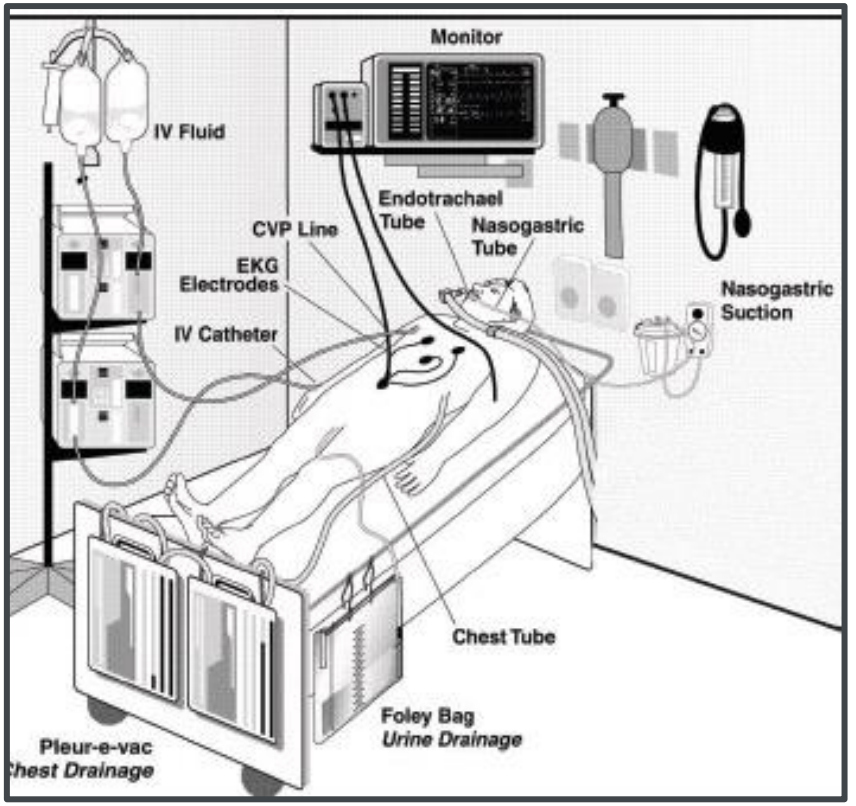
Acinetobacter baumannii, carbapenem-resistant

Driven by AB use and poor infection control

Healthcare Setting

Resistant to colistin in 4% of cases

Resilient



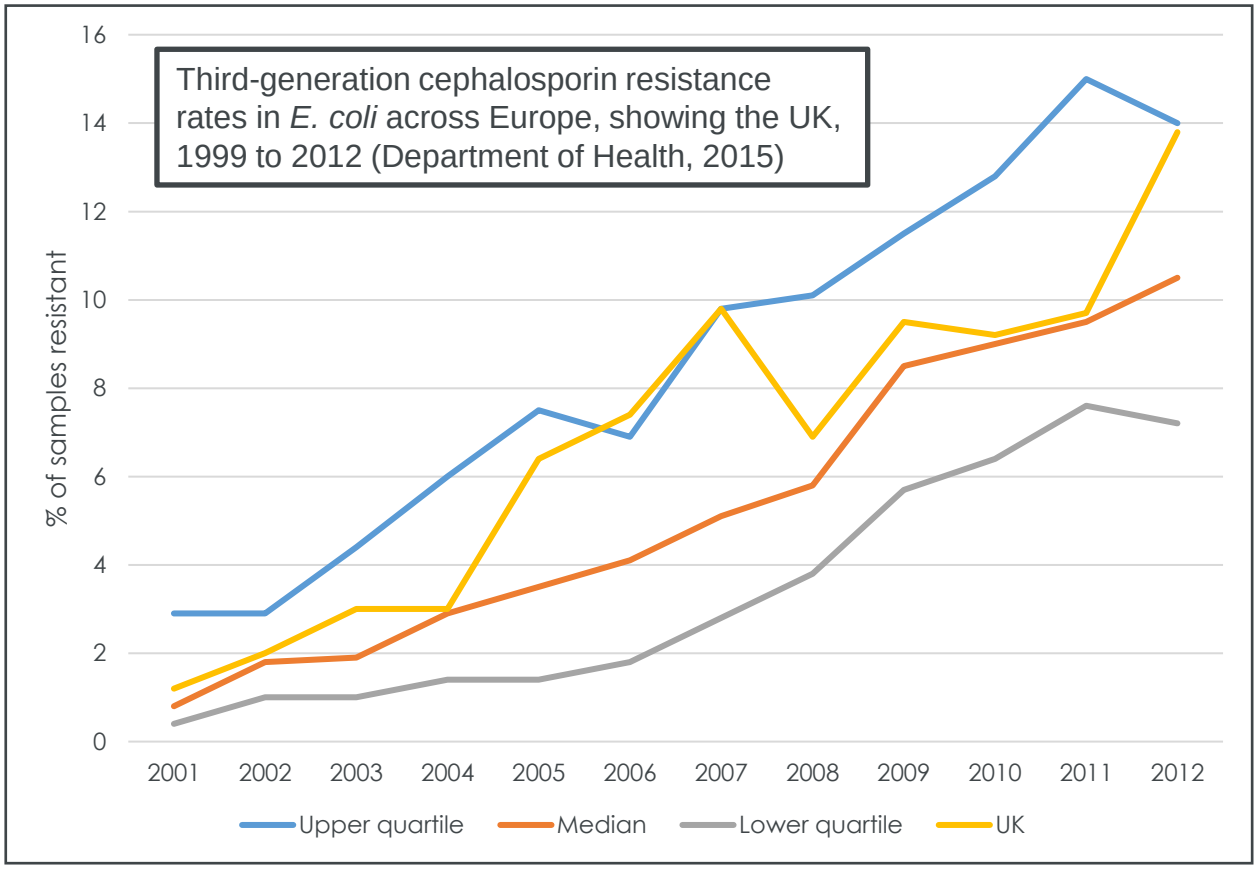
Institute and Faculty of Actuaries

Pseudomonas aeruginosa, carbapenem-resistant

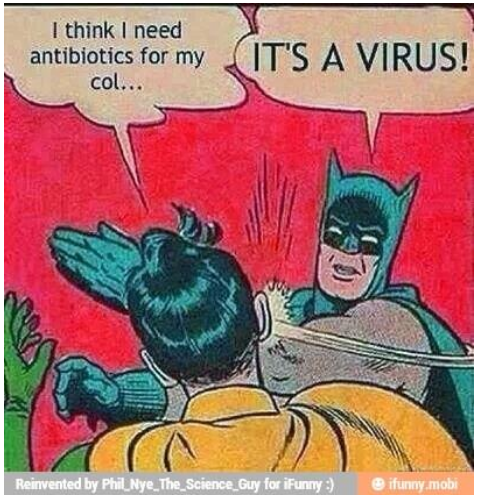
- Found widely in the environment
- Common cause of mild and serious infections
- Risk profile similar to A. Baumannii

Institute and Faculty of Actuaries

Enterobacteriaceae, carbapenem-resistant, 3rd generation cephalosporin-resistant



These bacteria are associated with higher frequency of inappropriate antimicrobial therapy, poorer clinical response, and longer length of hospital stay

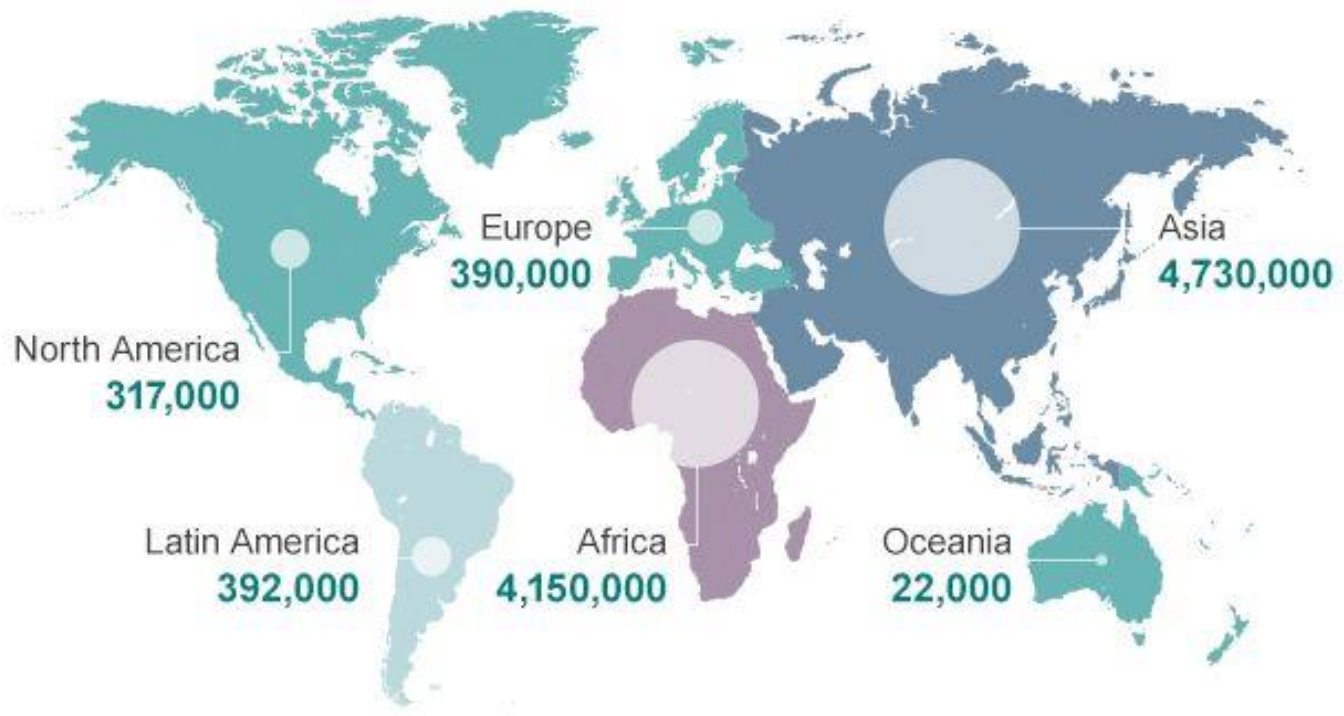


Institute and Faculty of Actuaries

…and why it is important?

"We have reached a critical point and must act now on a global scale to slow down antimicrobial resistance" – Professor Dame Sally Davies, UK Chief Medical Officer

Deaths attributable to antimicrobial resistance every year by 2050



Source: Review on Antimicrobial Resistance 2014

Tackling resistance takes a long time…

Changing behaviours

Developing new antibiotics

Institute and Faculty of Actuaries

Institute and Faculty of Actuaries

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-posi

Bradley M. Hover[1], Seong-Hwan Kim[1], Micah Katz[1], Zachary
Melinda A. T
and Sean F. E

Berglund *et al. Microbiome* (2017) 5:134
DOI 10.1186/s40168-017-0353-8

Microbiome

RCH

Open Access

CrossMark

ification of 76 novel B1 metallo-β-
mases through large-scale screening
nomic and metagenomic data

und[1,2], Nachiket P. Marathe[2,3], Tobias Österlund[1,2], Johan Bengtsson-Palme[2,3], Stathis Kotsakis[2,3],
Flach[2,3], D G Joakim Larsson[2,3] and Erik Kristiansson[1,2*]

n bad to worse, but we're
we're doing badly again."

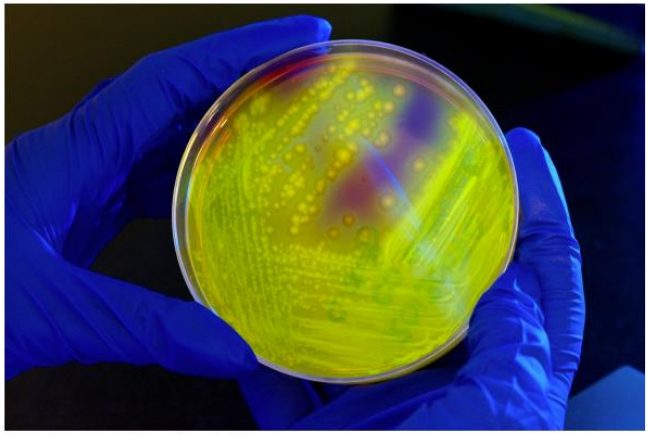
MIT Technology Review

Log In / Create an account Search Q

Topics+ The Download Magazine Events More+

Subscribe

Think Big. Take Risks. INNOVATE!
DISCOVER MORE ABOUT OUR DII R&D FUNDING 703.808.2769



Clostridium difficile bacteria in a petri dish, glowing under long-wave ultraviolet light.

Rewriting Life

Edible CRISPR Could Replace Antibiotics

Researchers are developing a probiotic to make disease-causing bacteria self-destruct.

Advertisement

EmTech HONG KONG
26 – 27 June 2018 • HKSTP
Featuring
GGV Capital Google
BOOK NOW!

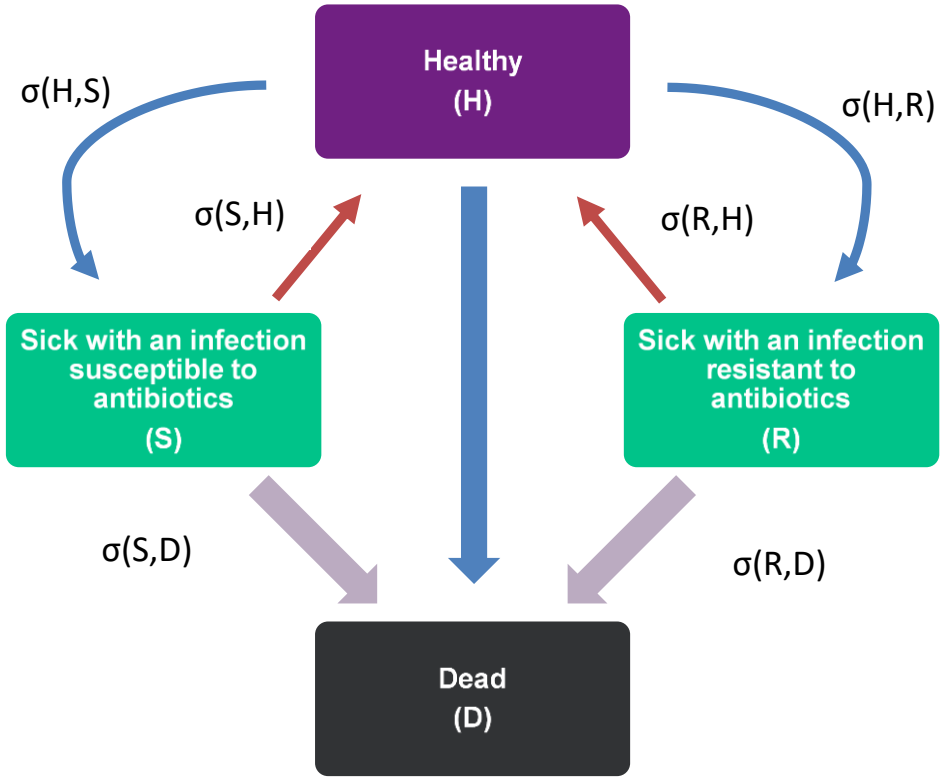
Institute and Faculty of Actuaries

Model structure and parameterisation

Ross Hamilton

June 11, 2024

How can we model this impact?



Modelling criteria

- Simplicity
- Availability of data
- Appropriate outputs

Basic structure decided on:

- Multi-state Markov model
- Calibrate to current observed levels of mortality and morbidity
- Project varying resistance over time and calculate the change in mortality and morbidity

Institute and Faculty of Actuaries

Data sources – what is available?

Public Health England

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Office for National Statistics

PLOS | Open for Discovery

- **Current and historical resistance profiles for *S. aureus*, *E. coli* and selected other infections vs various antibiotics**

Institute and Faculty of Actuaries

Data sources – what is available?

Public Health England

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Office for National Statistics

PLOS | Open for Discovery

- **Current and historical resistance profiles for *S. aureus*, *E. coli* and selected other infections vs various antibiotics.**
- Resistance is not absolute. Resistance can be to a single antibiotic, or multidrug resistance.
- Bias? Are samples more likely to be taken from the very ill? Will resistant strains be over-represented because of this?

Institute and Faculty of Actuaries

Data sources – what is available?

Public Health England

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Office for National Statistics

PLOS | Open for Discovery

- **Incidence rates for bacteraemias.**

Institute and Faculty of Actuaries

Data sources – what is available?

Public Health England

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Office for National Statistics

PLOS | Open for Discovery

- **Incidence rates for bacteraemias.**
- Limited data. *E. coli* monitoring in England goes back to 2013.
- Limited evidence for how resistance interacts with incidence.
- Bias? Monitoring is of HCAIs.

Institute and Faculty of Actuaries

Data sources – what is available?

Public Health England

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Office for National Statistics

PLOS | Open for Discovery

- **Death rates for bacteraemias.**

Institute and Faculty of Actuaries

Data sources – what is available?

Public Health England

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

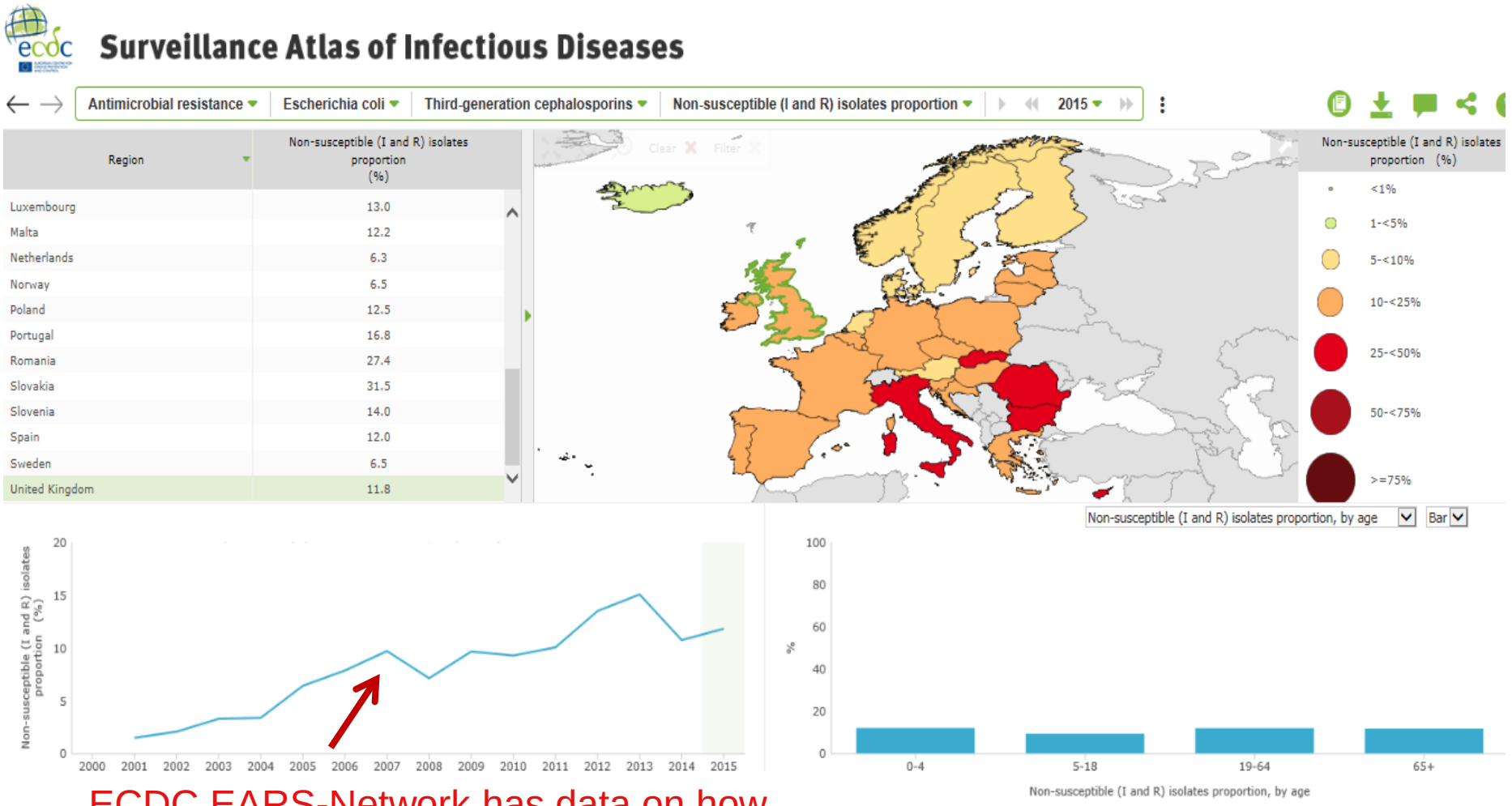
Office for National Statistics

PLOS | Open for Discovery

- **Death rates for bacteraemias.**
- Limited data. *E. coli* monitoring in England goes back to 2013.
- Granularity of data:
  - Confounding causes of death?
  - Academic literature is helpful here.
- Large error bounds around estimates of the relative virulence of resistant and susceptible strains.
- Bias? The most ill are more likely to be sampled.

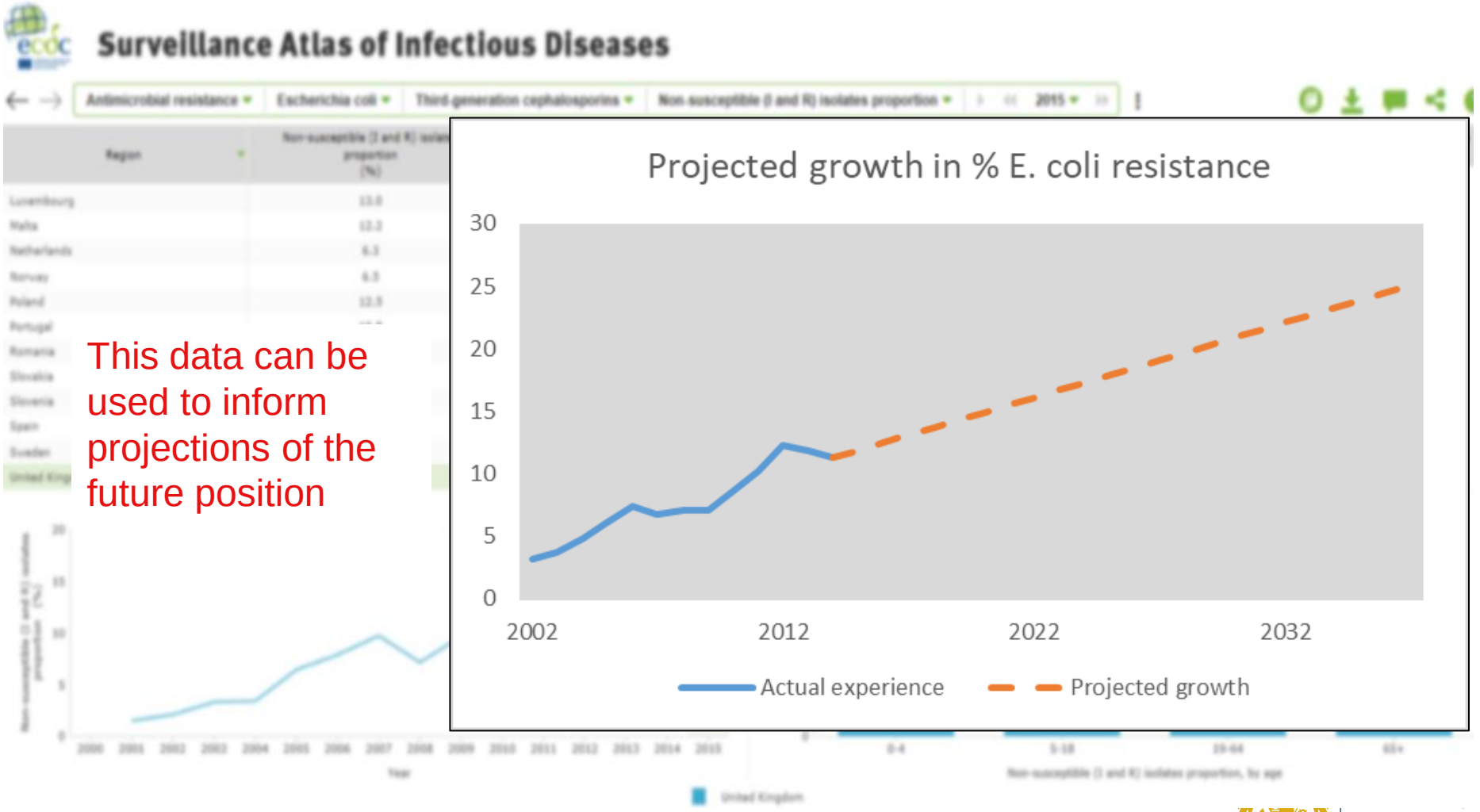
Institute and Faculty of Actuaries

Trends in resistance can be observed…



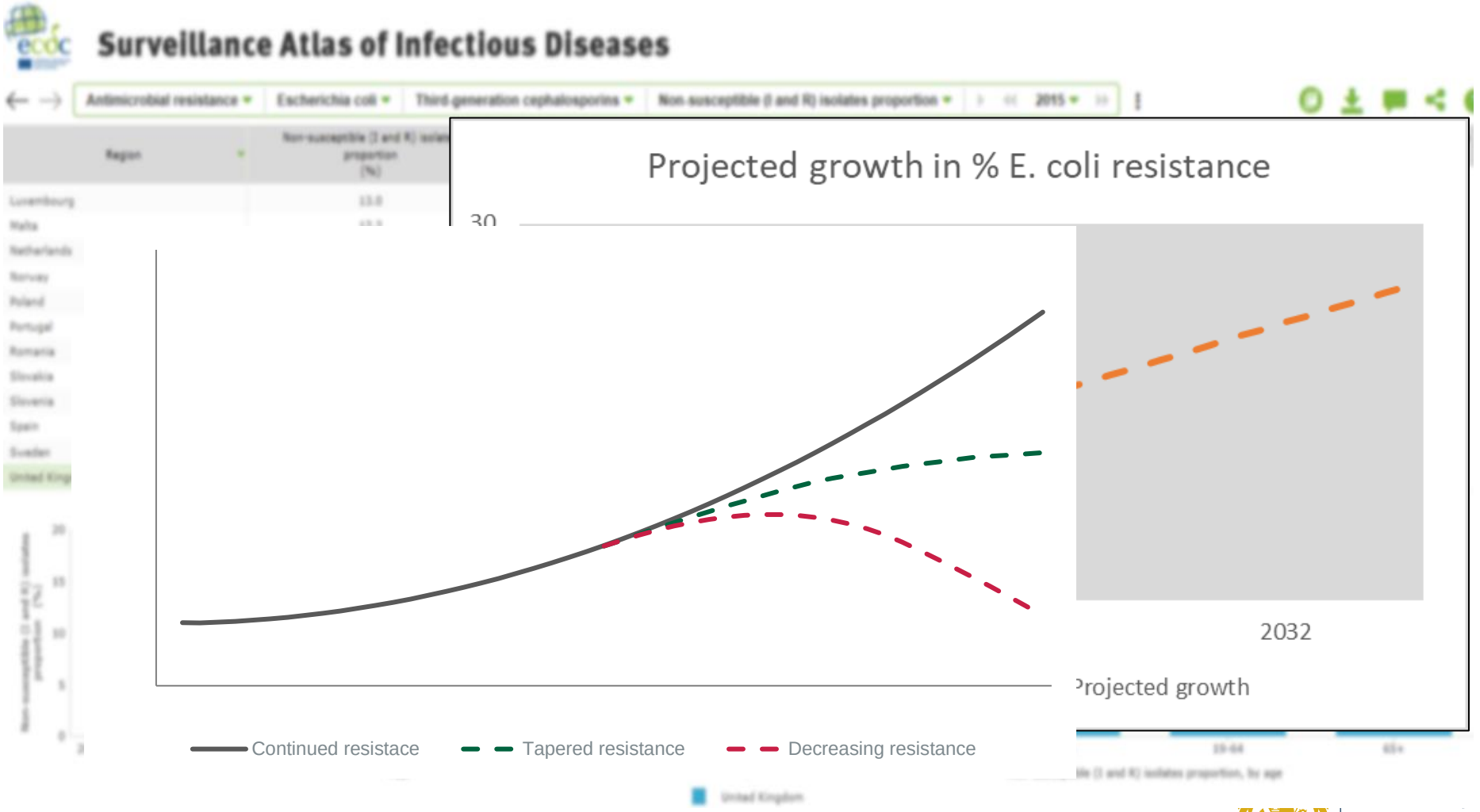
ECDC EARS-Network has data on how resistance has increased over time

…and extrapolated forwards



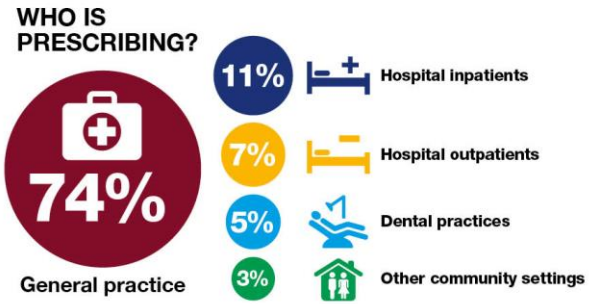
of Actuaries

…and extrapolated forwards



of Actuaries

Other considerations



30 years since a new class of antibiotics was last introduced….

Barriers to R&D Investment

Cautious optimism in 2 new compounds

Infographics sourced from "Review on Antimicrobial Resistance" 2014

Institute and Faculty of Actuaries

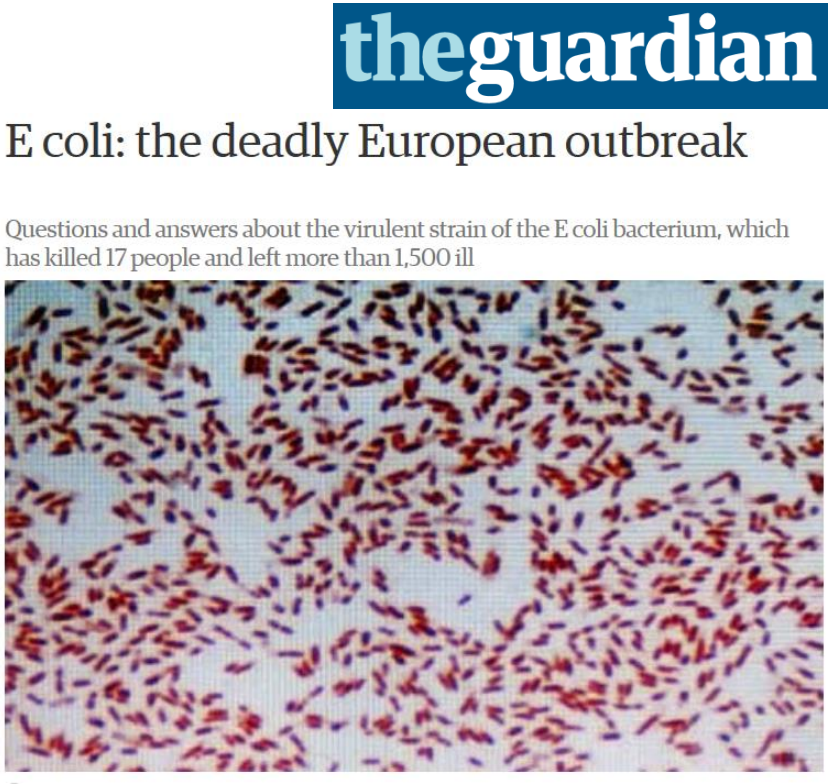
Institute and Faculty of Actuaries

‘Results’ and next steps

June 11, 2024

Example Results: *E. coli* resistance

- Initial example parameterisation based on:
  - Growth in *E. coli* bacteria resistant to 3rd generation cephalosporin antibiotics
  - Ages 19-64, i.e. working age population
  - Projected position in 2037, i.e. 20 years' time
- Under a plausible central scenario there would be a 1% uplift in overall mortality
- In an extreme scenario, based on 95% confidence level upper bound, there would be a 2-3% uplift in overall mortality
- And this is just for one strain of bacteria …
- Model will help actuaries understand the overall impact on mortality/morbidity and quantify the financial impact, even calibrating their own scenarios



Institute and Faculty of Actuaries

Working party – next steps

Sessional meeting February 2019

Model development

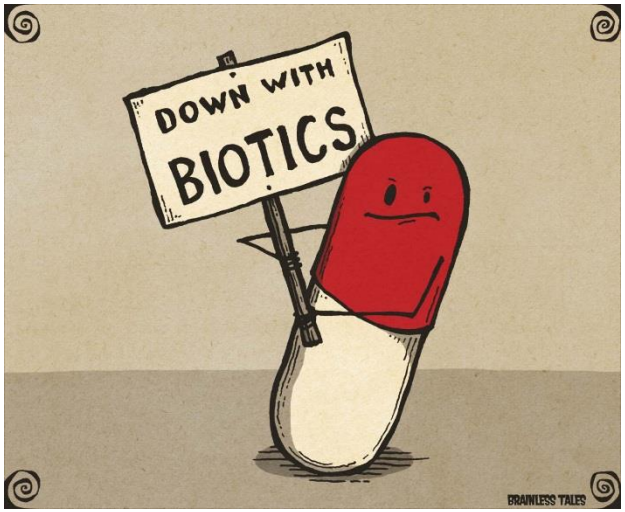
- Parameterisation – other main bacteria (5)
- Interactions between pathogens
- Validation / Documentation

- **Full model release**
- **Suggested parameterisation based on UK data**
- **Associated paper – main issues relating to sources of ABR, mitigation actions, recent trends, other projection results / methodologies, and background to our model and results from the model**

Institute and Faculty of Actuaries

Questions

Comments



Expressions of individual views by members of the Institute and Faculty of Actuaries and its staff are encouraged.

The views expressed in this presentation are those of the presenter.

Institute and Faculty of Actuaries