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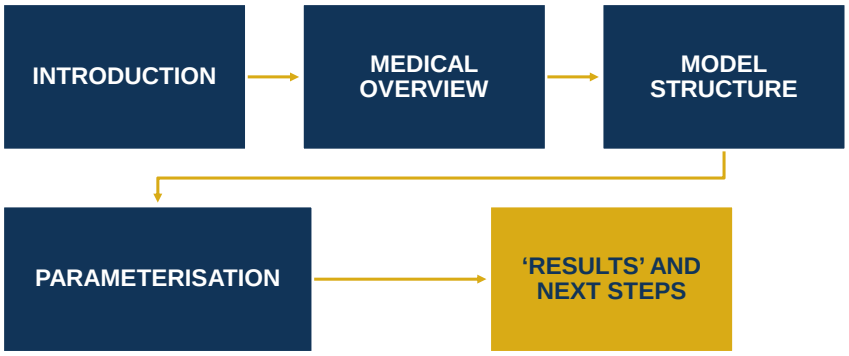
When the drugs don't work…

Matthew Edwards, Nicola Oliver and Sheridan Fitzgibbon (IFoA Antibiotic Resistance Working Party)

23 November 2017

Agenda



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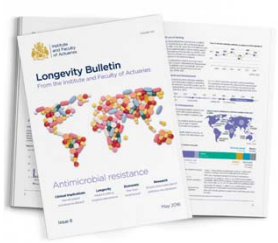
Working party background

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**

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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	Aviva
Ross Hamilton	Model development	Willis Towers Watson
Irene Merk	General	SCOR
Roshane Samarasekera	Model development	GAD
Soumi Sarkar	General	Legal & General
Katherine Fossett	General	Barnett Waddingham

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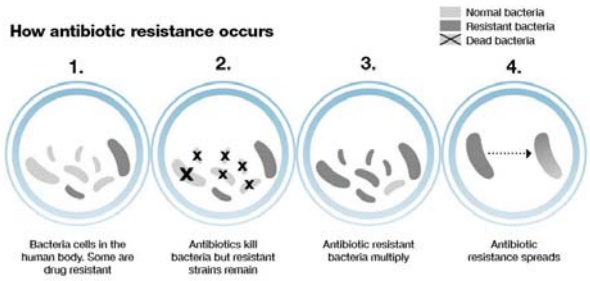
Medical overview

Nicola Oliver

17 November 2017

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

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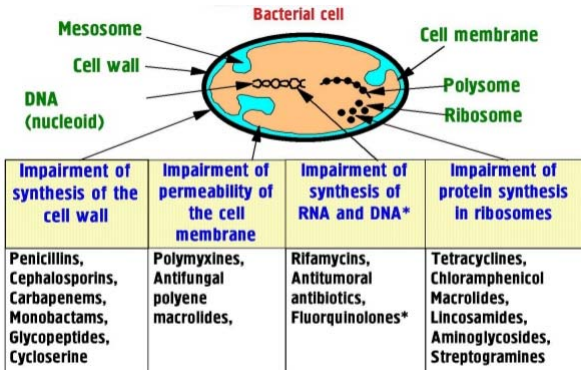
How does it actually work (the science!)



Impairment of synthesis of the cell wall	Impairment of permeability of the cell membrane	Impairment of synthesis of RNA and DNA*	Impairment of protein synthesis in ribosomes
Penicillins, Cephalosporins, Carbapenems, Monobactams, Glycopeptides, Cycloserine	Polymyxines, Antifungal polyene macrolides,	Rifamycins, Antitumoral antibiotics, Fluorquinolones*	Tetracyclines, Chloramphenicol Macrolides, Lincosamides, Aminoglycosides, Streptogramines

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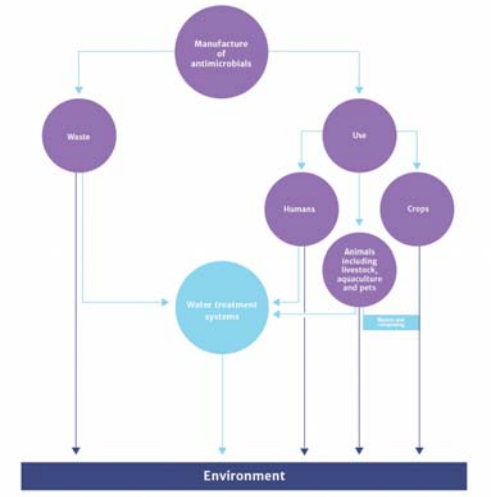
What are the sources of resistance?

Sources of resistance



How animals can pass on resistant bacteria

Infographics sourced from "Review on Antimicrobial Resistance" 2014

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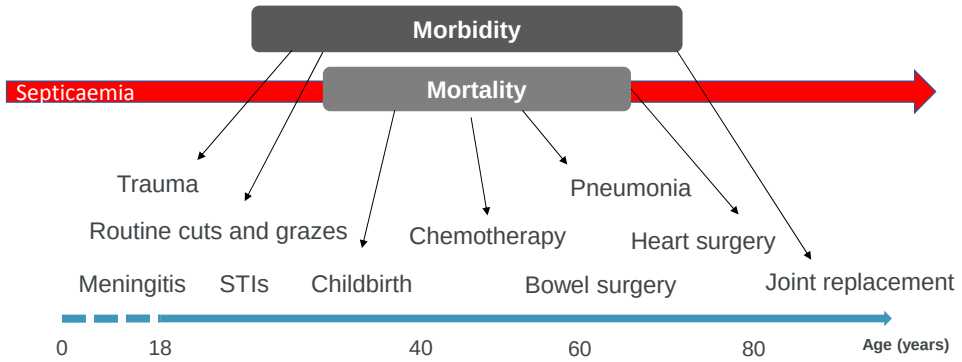
How does ABR affect people and our work?



Change insurance products?

Revised pricing of existing insurance?

Pension fund reserves over-estimated?

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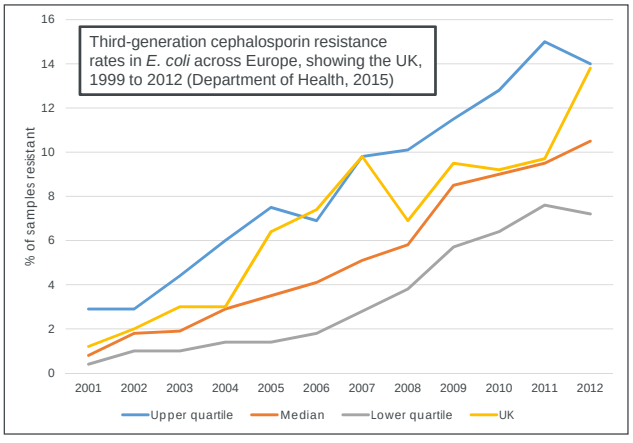
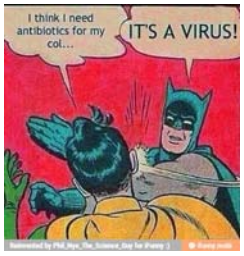
Trends in resistance…



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



What is the actuarial response to these trends… model it!

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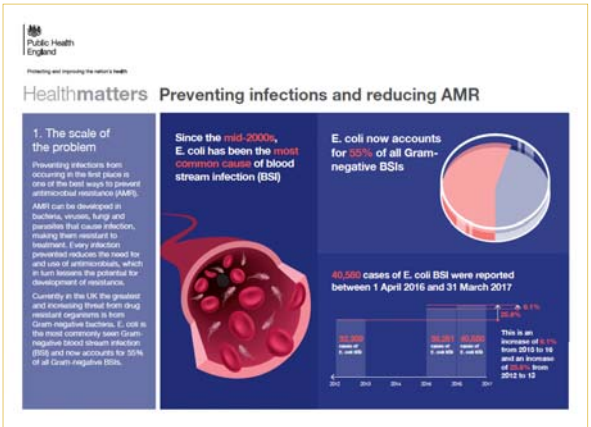

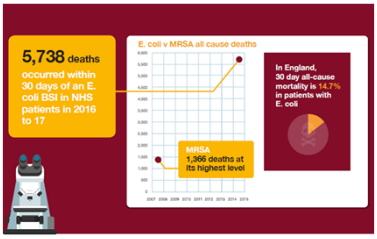

E. Coli current cause of concern for Public Health England, so plenty of available data to play with…..

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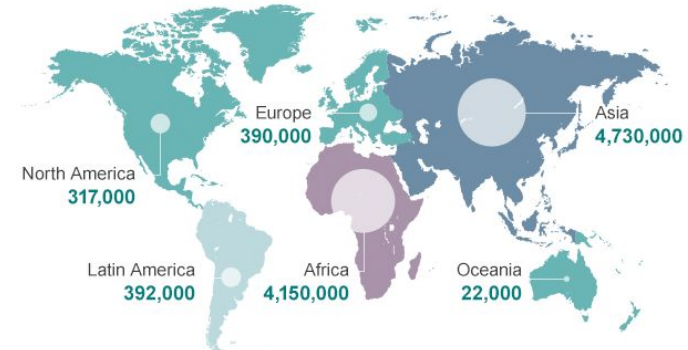
…and why it is important?

"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

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Model structure and parameterisation

Sheridan Fitzgibbon

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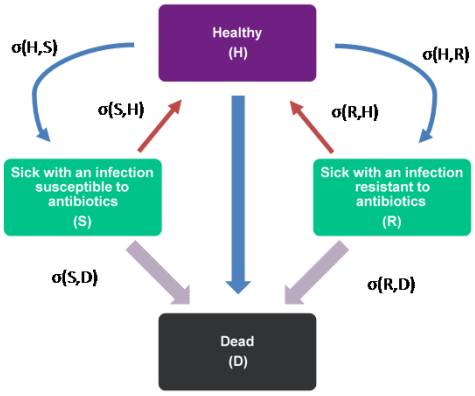
How can we model this impact?



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

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Data sources – what is available?

Public Health England

ecdc

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**

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Data sources – what is available?

Public Health England

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- **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?

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Data sources – what is available?

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PLOS | Open for Discovery

- **Incidence rates for bacteraemias.**

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Data sources – what is available?

Public Health England

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- **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.

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Data sources – what is available?

Public Health England

ecdc

Office for National Statistics

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- **Death rates for bacteraemias.**

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Data sources – what is available?

Public Health England

ecdc

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.

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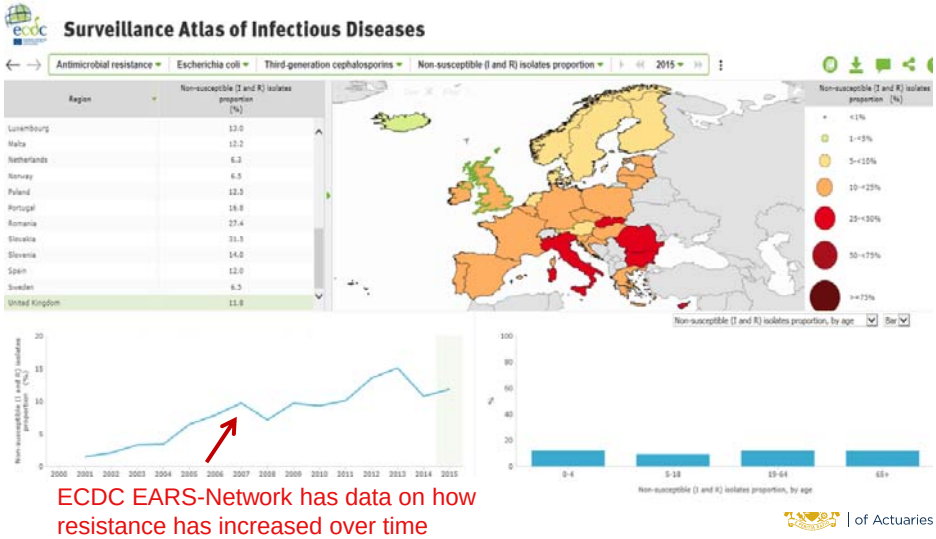
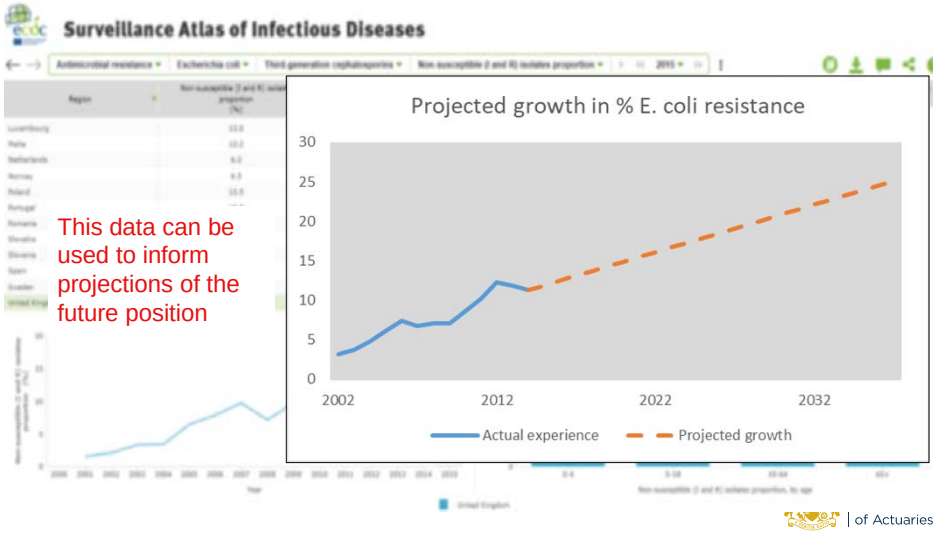
Trends in resistance can be observed…



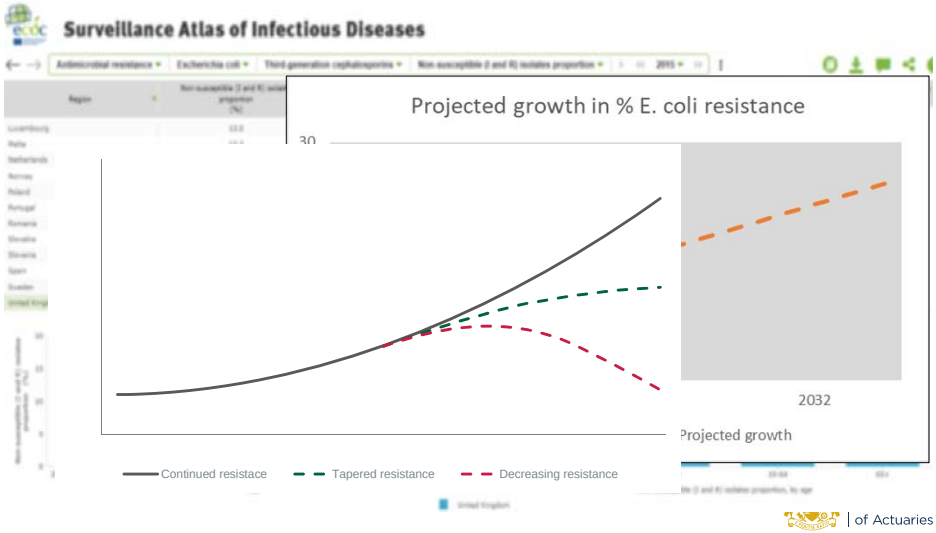
ECDC EARS-Network has data on how resistance has increased over time

…and extrapolated forwards



This data can be used to inform projections of the future position

…and extrapolated forwards



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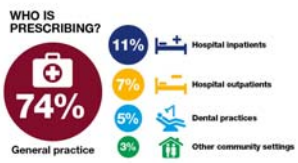
Other considerations



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

Barriers to R&D Investment

Cautious optimism in 2 new compounds

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Infographics sourced from "Review on Antimicrobial Resistance" 2014

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‘Results’ and next steps

Matthew Edwards

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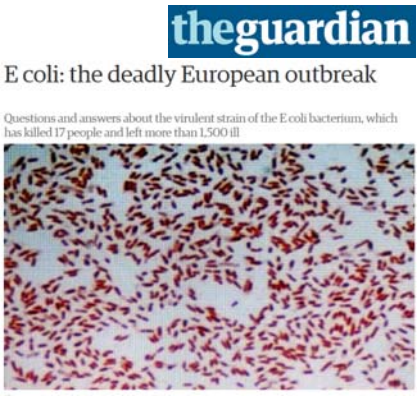
Example Results: *E. coli* resistant to 3rd generation cephalosporins

- 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]% annual uplift in overall mortality
- In an extreme scenario, based on 95% confidence level upper bound, there would be a [2-3]% annual 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



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Working party – next steps

ABR Event
Staple Inn
April 2018

Model development

- Move to matrix method
- Parameterisation – other main bacteria (5?)
- 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**

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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.

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