Hopes, Hypes and Multivallate Defences Against Antimicrobial Resistance
Professor Neil Woodford, Public Health England
Denver Russell Memorial Teleclass

Public Health England

Denver Russell Memorial Teleclass Lecture

Hopes, hypes and multivallate defences against antimicrobial resistance

Professor Neil Woodford (@Prof_Neil)
Antimicrobial Resistance & Healthcare Associated Infections (AMRHAI) Reference Unit

Hosted by Prof. Jean-Yves Maillard
Cardiff University, Wales

www.webbertraining.com
April 10, 2018

Public Health England

Links between AMR …and Badbury Rings (Dorset) ?

http://www.castlesfortsbattles.co.uk

- a multivallate iron age hillfort
- layers of challenging defence
- …, but not impregnable !

A Webber Training Teleclass
Hosted by Prof. Jean-Yves Maillard, Cardiff University, Wales
www.webbertraining.com

Public Health England

The UK's long record of high-level leadership

- AMR has a cyclical history
- hard now to be genuinely original
- much done, thought or written before
- recurring losses of momentum, necessitating new waves of activity

3 Webber Training Teleclass, 10th April 2018 © Crown Copyright

Jim O'Neill's *Review on AMR*

Commissioned by the UK Prime Minister, July 2014 *to revitalize antibiotic discovery – focused on economics*.

"Drug-resistant infections already kill hundreds of thousands a year globally, and by 2050 that figure could be more than 10 million. The economic cost will also be significant, with the world economy being hit by up to $100 trillion by 2050 if we do not take action."

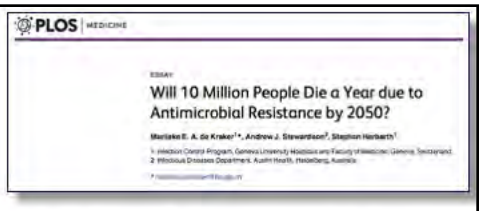
www.amr-review.org, 2015

Review on Antimicrobial Resistance
Tackling drug-resistant infections globally

Webber Training Teleclass, 10th April 2018 © Crown Copyright 4

Public Health England

Scientists kick back, 2016


PLOS | MEDICINE

Will 10 Million People Die a Year due to Antimicrobial Resistance by 2050?

"*There is undoubtedly a large clinical and public health burden associated with AMR, but it is challenging to quantify the associated excess morbidity and mortality.*"

"*Current global estimates of the burden of AMR are not very informative; we need detailed, reliable data to be able to improve AMR control measures, preferably based on comprehensive, population-based surveillance data from low-, middle-, and high- income countries.*"

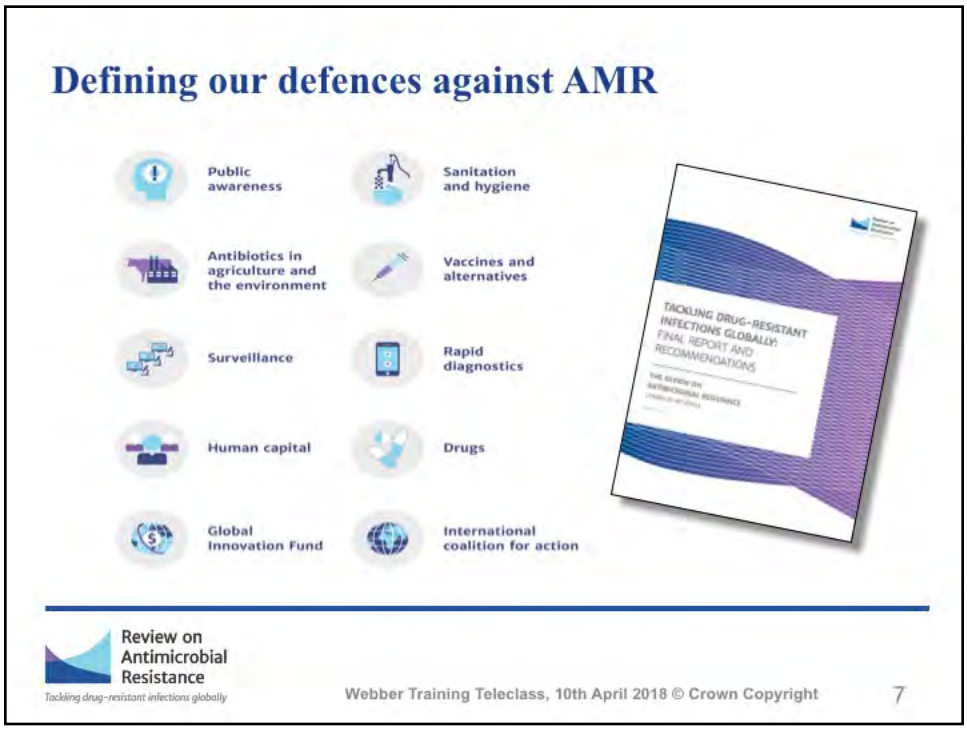
The art of predicting "broad brush estimates" of people dying from AMR

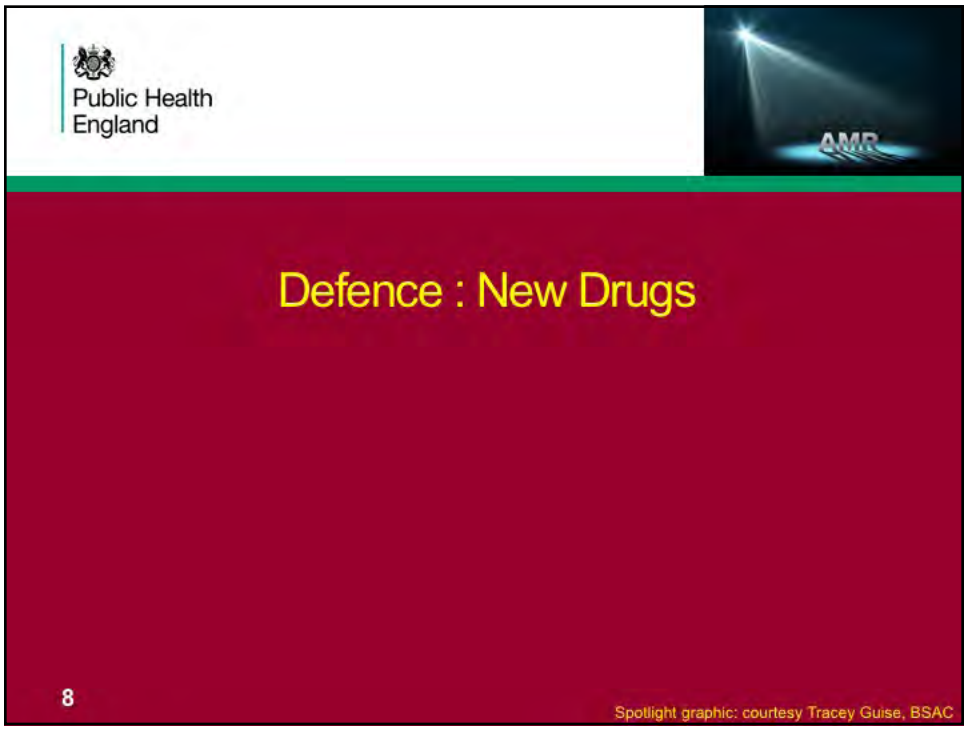
"*The AMR Review even acknowledged "that the reported numbers are "broad brush estimates," […] that "more detailed and robust work will no doubt be done by academic researchers," and that there is a lack of data, urging for improvement of infection surveillance."*

Public Health England

Global commitment to combat AMR

- WHA 2014 resolution
- WHO Global AMR Action Plan 2015 – *framework for action*
- Global Health Security Agenda: AMR action package - *mechanism and collaboration to accelerate implementation*
- Many other national action plans
- UNGA, 2016
- UN Inter-Agency Coordination Group, 2017


Defining our defences against AMR
Public awareness
Sanitation and hygiene
Antibiotics in agriculture and the environment
Vaccines and alternatives
Surveillance
Rapid diagnostics
Human capital
Drugs
Global Innovation Fund
International coalition for action
TACKLING DRUG-RESISTANT INFECTIONS GLOBALLY: FINAL REPORT AND RECOMMENDATIONS
Review on Antimicrobial Resistance
Tackling drug-resistant infections globally
Webber Training Teleclass, 10th April 2018 © Crown Copyright
7


Public Health England
AMR
Defence : New Drugs
8
Spotlight graphic: courtesy Tracey Guise, BSAC

Public Health England

Countering the problem - then and now

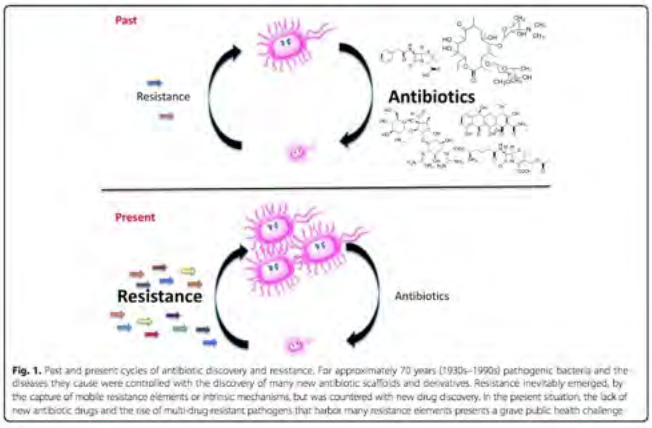


Fig. 1. Past and present cycles of antibiotic discovery and resistance. For approximately 70 years (1930s–1990s) pathogenic bacteria and the diseases they cause were controlled with the discovery of many new antibiotic scaffolds and derivatives. Resistance inevitably emerged, by the capture of mobile resistance elements or intrinsic mechanisms, but was countered with new drug discovery. In the present situation, the lack of new antibiotic drugs and the rise of multi-drug resistant pathogens that harbor many resistance elements presents a grave public health challenge

9 Webber Training Teleclass, 10th April 2018 © Crown Copyright Waglechner & Wright BMC Biology 2017

Public Health England

We don't have enough antibiotics in development to tackle the resistance issues we face *now*

…and the success of those in development is not guaranteed

10 Spotlight graphic: courtesy Tracey Guise, BSAC

Public Health England

WHO Priority Pathogens list

- antibiotics specifically active against multidrug- and extensively drug-resistant Gram-negative bacteria.
- antibiotics for the paediatric population and for oral formulations for community diseases with a high morbidity burden such as drug-resistant *Neisseria gonorrhoeae*, *Salmonella typhi* and ESBL-producing *Enterobacteriaceae*.
- new classes of antibiotics without cross- and co-resistance to existing classes should be supported.
- must also reduce the burden of infections e.g. increased vaccination coverage, improved sanitation or sustained implementation of infection control measures

Priority 1: CRITICAL*

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

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

Priority 2: HIGH

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella spp., fluoroquinolone-resistant

Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

Streptococcus pneumoniae, penicillin-non-susceptible

Haemophilus influenzae, ampicillin-resistant

Shigella spp., fluoroquinolone-resistant

Mycobacteria (including *Mycobacterium tuberculosis*, the cause of human tuberculosis), w subjected to review for inclusion in this prioritization exercise as it is already a globally estab priority for which innovative new treatments are urgently needed.

* Enterobacteriaceae include: *Klebsiella pneumonia*, *Escherichia coli*, *Enterobacter* spp., *Serrati Proteus* spp., and *Providencia* spp. *Morganella* spp.

www.who.int/medicines/publications/WHO-PPL-Short_Summary_25Feb-ET_NM_WHO.pdf

11 Webber Training Teleclass, 10th April 2018 © Crown Copyright

Public Health England

New anti-Gram-negatives

Name	Phase	Company	Class
Ceftolozane+ tazobactam	FDA approved Dec 19, 2014	Merck	Novel cephalosporin + beta-lactamase inhibitor
Ceftazidime+ avibactam	FDA approved Feb 25, 2015	Pfizer / Allergan	Cephalosporin + novel beta-lactamase inhibitor
Meropenem+ vaborbactam	FDA approved Aug 29 2017	The Medicines Company	Meropenem + novel beta-lactamase inhibitor

12 Webber Training Teleclass, 10th April 2018 © Crown Copyright

www.pewtrusts.org
www.drugs.com

Public Health England

Most CPE are multi-resistant, 2016

Antibiotic	Proportion of susceptibility, % (n=708)								
	metallo-enzyme producers (NDM,VIM, IMP) (n=261)			non-metallo-enzyme producers (KPC, OXA-48-like, KPC + OXA-48-like, GES, IMI, SME, FRI-2) (n=422)			others (MBL + non-metallo-enzyme: NDM + OXA-48-like) (n=25)		
	E. coli	*Klebsiella spp.*	*Enterobacter /Citrobacter*	*E. coli*	*Klebsiella spp.*	*Enterobacter /Citrobacter*	*E. coli*	*Klebsiella spp.*	*Enterobacter /Citrobacter*
Imipenem (IPM) (S <=2 mg/L)	5	3	8	83	42	42	0	0	0
Meropenem (S <=2 mg/L)	5	3	8	87	40	44	0	0	0
Ertapenem (S <=0.5 mg/L)	0	0	0	3	1	0	0	0	0
Ampicillin (S <=8 mg/L)	0	0	0	0	0	0	0	0	0
Co-amoxiclav (S <=8 mg/L)	0	0	0	0	0	0	0	0	0
PIP-tazobactam (S <=8 mg/L)	4	0	0	8	0	1	0	0	0
Cefotaxime (S <=1 mg/L)	0	0	0	29	11	0	0	0	0
Ceftazidime (CAZ) (S <=1 mg/L)	0	0	0	40	19	23	0	0	0
CAZ-avibactam (S <=8 mg/L)	0	0	0	98	96	96	0	0	0
Ceftolozane-tazobactam (S <=1 mg/L)	0	0	0	52	17	10	0	0	0
Aztreonam (S <=1 mg/L)	20	28	48	48	20	10	0	0	100
Ciprofloxacin (S <=0.25 mg/L)	5	7	18	46	26	33	0	0	0
Gentamicin (S <=2 mg/L)	59	23	20	62	58	61	0	5	100
Tobramycin (S <=2 mg/L)	28	4	5	61	42	56	0	0	100
Amikacin (S <=8 mg/L)	90	46	55	92	68	89	100	4	100
Colistin (S <=2 mg/L)	97	93	97	98	84	93	100	64	100
Tigecycline (S <=1 mg/L)	96	61	88	98	64	84	100	36	100
Total number	78	123	60	133	200	89	2	22	1

active in vitro against <=50% isolates
active in vitro against 50-90% isolates
active in vitro against >90% isolates

a = two isolates susceptible to avibactam alone

13 Webber Training Teleclass, 10th April 2018 © Crown Copyright AMRHAI, unpublished data

Public Health England

Developmental anti-Gram-negatives, May 2017

Name	Phase	Company	Class
IPM + relebactam	Phase 3	Merck	Carbapenem + novel beta-lactamase inhibitor
Cefiderocol (S649266)	Phase 3	Shionogi	Siderophore cephalosporin
Omadacycline	Phase 3	Paratek	Tetracycline
Eravacycline	Phase 3	Tetraphase	Tetracycline
Plazomicin	Phase 3	Achaogen	Aminoglycoside

14 Webber Training Teleclass, 10th April 2018 © Crown Copyright www.pewtrusts.org

Public Health England

Assessing the potential of the antibiotic pipeline - I

Urgent threat pathogens

The Centers for Disease Control and Prevention considers three bacteria to be urgent threats to public health.[4] While a number of promising antibiotics with the potential to treat infections caused by these bacteria are in the pipeline, more drug candidates are needed to meet current and future patient needs.

3 antibiotics are in development to treat drug-resistant gonorrhea infections. An estimated 246,000 drug-resistant cases occur in the United States each year.[5]

6 antibiotics are in development to treat patients with *Clostridium difficile* infections, which can sometimes result in life-threatening diarrhea. The CDC estimates that nearly 500,000 Americans acquired *C. difficile* infections in 2011; 15,000 of them died as a result.[6]

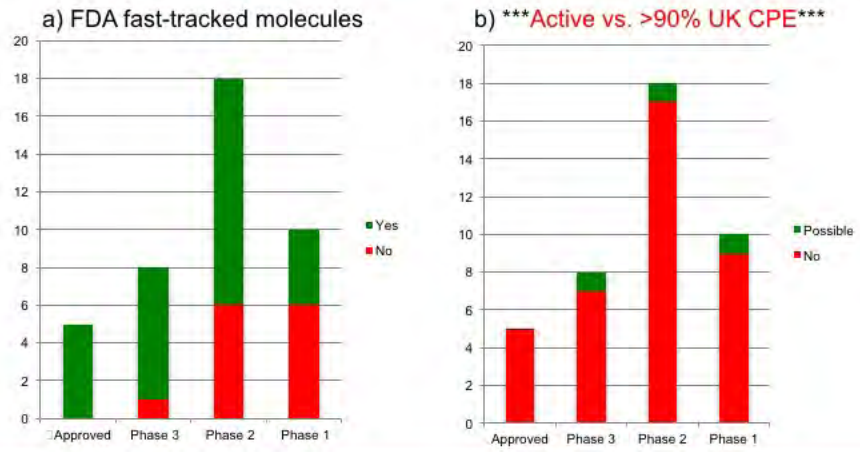
7 or more antibiotics are in development with the potential to treat infections caused by carbapenem-resistant Enterobacteriaceae (CRE). Infections caused by this resistant pathogen can kill up to 50 percent of patients if the bacteria infect the bloodstream.[7]

NOTE: This infographic is based on analysis as of March 2017.

15 Webber Training Teleclass, 10th April 2018 © Crown Copyright — Analysis of data from www.pewtrusts.org

Public Health England

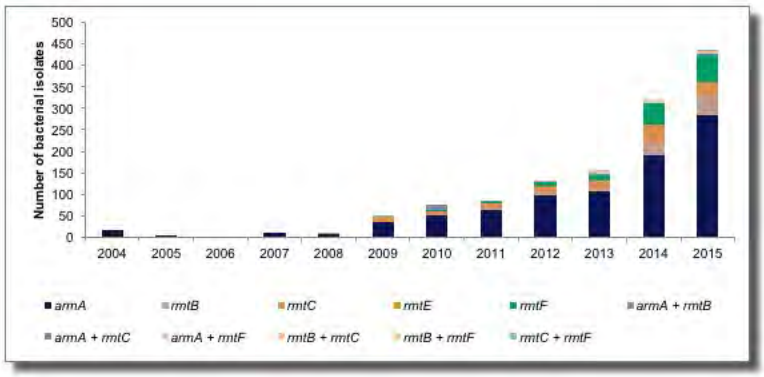
Assessing the potential of the antibiotic pipeline - II



16 Webber Training Teleclass, 10th April 2018 © Crown Copyright — Analysis of data from www.pewtrusts.org

Public Health England

Example: pan-aminoglycoside resistance (incl. plazomicin) in the UK



 Emma Taylor *et al.*, ECCMID, 2017

Public Health England

Association of RMTases with carbapenemases

RMTase	NDM*	OXA-48-like*	NDM + OXA-48-like	Other	Total
armA	140	22	17	3	182 (46%)
rmtB	43	2	8	2	55 (14%)
rmtC	51	1	11	0	63 (16%)
rmtD	0	0	0	1	1
rmtF	28	47	3	0	78 (20%)
2 RMTases	7	7	3	0	17 (4%)
Total (% +ve)	269 (57%)	79 (11%)	42 (82%)	6 (1%)	396 (21%)
RMTase -ve	207	642	9	624	1482

c. 98% have NDM and / or OXA-48 like enzymes

 Emma Taylor *et al.*, ECCMID, 2017

Public Health England

Assessing the potential of the antibiotic pipeline - III

A GO / NO GO decision: Delafloxacin Stumbles in Gonorrhea Study

February 2, 2015 by Herald – No Comments ↓

The treatment history of N. gonorrhoeae makes for fascinating reading. This organism has always been able to keep the upper hand in the war of tug versus drug. Once susceptible to sulfa drugs, to penicillin, tetracyclines and fluoroquinolones, it sequentially become resistant in the matter of a decade to every class of drug. At one time it looked like the organism would become PCN-susceptible again but that hope did not really materialize. Hence, we are all a bit nervous about the time when ceftriaxone loses its efficacy.

Now we hear that delafloxacin, a promising new fluoroquinolone, did not make the grade. According to a recent press release, Melinta (formerly Rib-X) had to stop the Phase 3 gonorrhea study for reasons of "insufficient efficacy".[1]

Cempra's solithromycin fails to match standard of care in GC study, development in NASH suspended; shares ease 10% premarket

- Cempra (NASDAQ:CEMP) is down 10% premarket on light volume in response to its announcement that a Phase 3 clinical trial, SOLITAIRE-U, assessing lead product candidate solithromycin compared to standard of care (intramuscular ceftriaxone plus oral azithromycin) for the treatment of uncomplicated genitourinary gonorrhea (GC) with or without concomitant chlamydia infection failed to demonstrate the non-inferiority of solithromycin. The success rates for standard of care were 84.5% in microbiological intent-to-treat population and 100% in microbiologically evaluable population compared to 80.5% and 91.3%, respectively, for solithromycin.

19 Webber Training Teleclass, 10th April 2018 © Crown Copyright

www.allphasepharma.com
www.seekingalpha.com

Public Health England

Too much publicity may be a bad thing

thebmjopinion Latest Authors Topics

Anthony McDonnell and Neil Woodford: Hype can undermine hope for new antibiotics

January 22, 2018

Every time a newly discovered molecule or preclinical drug makes the headlines as a "cure for drug resistant infections," we risk people thinking that the problem has been solved

Winning the "battle" against drug resistant infections will require new antibiotics, as well as public and professional behavioural change, better diagnostics, hygiene practices, and vaccines—all to either reduce unnecessary antibiotic use or to limit the spread of infections. No single new antibiotic is going to completely solve the problem of resistant infections, nor are most of the antibiotics in the early stages of development likely to make it to market.

Yet researchers often tout early stage successes in antibiotic development to the media as being potential game changers in preventing resistant infections. These statements are often misguided. Furthermore, they may undermine wider policy efforts to improve the research and development system for antibiotics because they create the impression that our current research system is adequate.

20 Webber Training Teleclass, 10th April 2018 © Crown Copyright

Public Health England

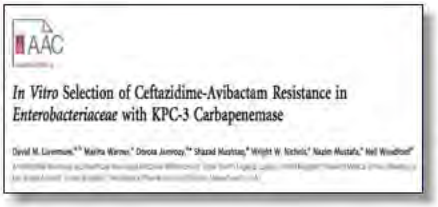
Resistance to new agents: never say 'never' !

"Now, here, you see, it takes all the running you can do, to keep in the same place."

Public Health England

Bacteria can be made resistant…

- In the lab:


AAC

In Vitro Selection of Ceftazidime-Avibactam Resistance in *Enterobacteriaceae* with KPC-3 Carbapenemase

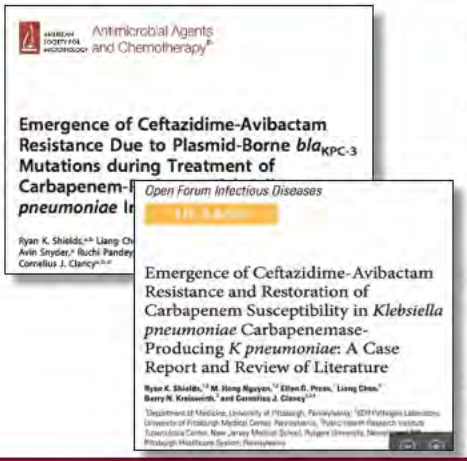
- An ICAAC 'top 10 beta-lactamase' paper

- In-vitro selection of CAZ-AVI mutants of *E. cloacae* and *K. pneumoniae*, all with the KPC-3 enzyme.
- CAZ-AVI mutants at up to 16 x MIC, with frequencies of ca. 10^{-9}
- CAZ MICs rose; MICs of carbapenems, other cephalosporins and PTZ reduced
- The most frequent change was Asp179Tyr, increasing CAZ specificity
- Clinical relevance uncertain

Livermore et al. 2015; 59:5324-30

Public Health England

…or can become resistant in the clinic

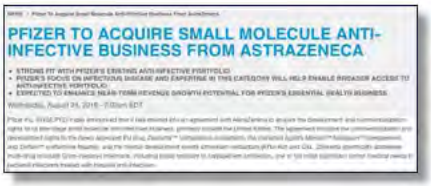


- Clinical failure of CAZ-AVI in 10/37 CPE patients
- CAZ-AVI-R *K. pneumoniae* from three patients after CAZ-AVI for 10-19 d.
- D179Y/T243M, D179Y or V240G mutations in bla_{KPC-3}, which were not present in baseline isolates
- MEM-S phenotype restored in *K. pneumoniae* from two patients; clinical successful R_x in one case
- clinical impact of CAZ-AVI-R may be ameliorated if carbapenem-S is restored

Shields et al. CID 2016; 63:1615-8
Shields et al. AAC 2017; 61. pii: e02097-16

Public Health England

New drugs, but the companies still pass the baton



Securing new drugs

- **More predictable market to make antibiotics R&D commercially sustainable**
  - lump-sum payments for 'successful' drugs
  - 'de-link' profitability from sales
- **jump-start a new innovation cycle in antibiotics**
  - Global AMR Innovation Fund
  - boost early-stage R&D into drugs and diagnostics
- **reduce barriers to drug development**
  - lower costs
  - improve the efficiency of research
  - lower global regulatory barriers

Review on Antimicrobial Resistance
Tackling drug-resistant infections globally

Public Health England

Need a more balanced reimbursement 'ecology'

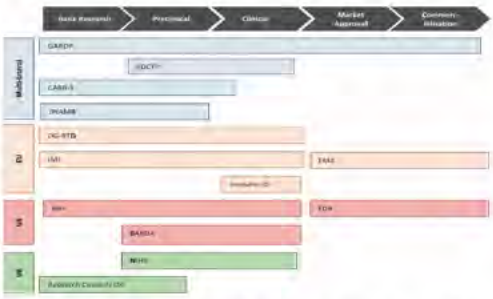


Table 2 Active initiatives based on their underlying incentives

	Only push incentives	Only outcome-based pull incentives	Only legislatory regulatory incentives	A hybrid of push-pull incentives
Multilateral	4	0	0	1
EU level	3	0	1	0
USA	1	0	1	1
UK	2	0	0	0
Total	10	0	2	2
Percent of total	71.4%	0.0%	14.3%	14.3%

- *overly committed to early-stage push funding*
- *limited late-stage push funding for clinical development*
- *almost no pull incentives to facilitate transition […] to commercialisation*

Simpkin *et al. J Antibiotics* 2017

Public Health England

New drug development vs. focus on antibiotic stewardship

- Not mutually exclusive
- In the future, new antibiotics must be viewed differently
  - not regarded as 'cure more' replacements by prescribers
  - not regarded as market blockbusters by manufacturers
- Changes in behaviour and expectation are essential
- ***This must be underpinned by better and faster diagnostics***
  - old drugs should be used for 'susceptible infections'
  - new drugs must be held in reserve for 'resistant infections'

27 Webber Training Teleclass, 10th April 2018 © Crown Copyright

Public Health England

Defence : New Diagnostics

28

Spotlight graphic: courtesy Tracey Guise, BSAC

Public Health England

Why new AMR diagnostics ?

- Prescribers must know earlier and more often that the infecting bacteria are susceptible to the drug they intend to use
  - Reduce empirical, broad-spectrum prescribing
- We need instruments and tests that can be deployed widely throughout the developed and developing world
- These new generations of diagnostics for AMR will facilitate
  - improved antibiotic stewardship
  - improved individual patient management
  - reduced onwards transmission of resistant bacteria

Public Health England

A recent UK analysis

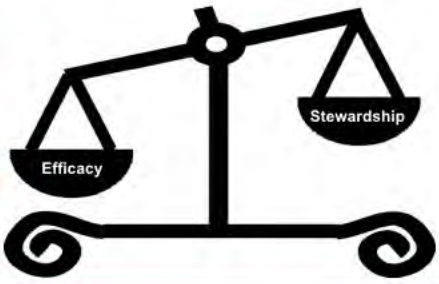
"…many technologies are stuck at the laboratory phase or, having developed technical accuracy, *have not progressed to clinical trials that provide cost-effectiveness and ultimately influence practice*."

Products are too often "pushed' by industry, not "pulled" by clinicians

Public Health England

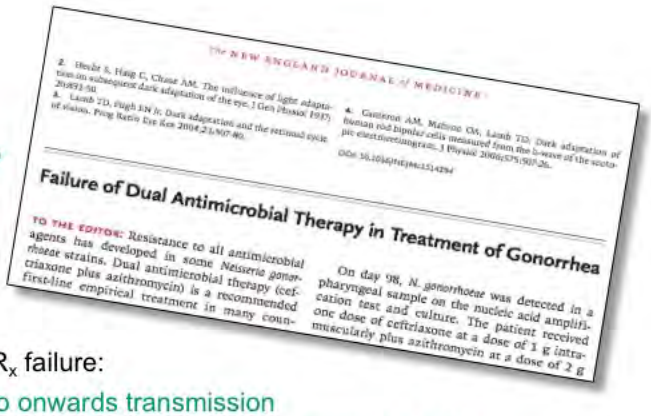
Gonorrhoea: a paradigm for better AMR diagnostics

- International approach to treatment
- Recommendation changes when resistance rate exceeds 5%
- Many patients are over-treated to prevent under-treating a few
- Gonococci in UK (2016):
  - >85% are PEN-susceptible
  - >65% are CIP-susceptible
- Neither drug is used
- Can't detect AMR at presentation



Public Health England

N. gonorrhoeae



THE NEW ENGLAND JOURNAL of MEDICINE

Failure of Dual Antimicrobial Therapy in Treatment of Gonorrhea

TO THE EDITOR: Resistance to all antimicrobial agents has developed in some *Neisseria gonorrhoeae* strains. Dual antimicrobial therapy (ceftriaxone plus azithromycin) is a recommended first-line empirical treatment in many coun-

On day 98, *N. gonorrhoeae* was detected in a pharyngeal sample on the nucleic acid amplification test and culture. The patient received one dose of ceftriaxone at a dose of 1 g intramuscularly plus azithromycin at a dose of 2 g

- World's first dual R_x failure:
  - Single case, no onwards transmission
  - MICs, CTR 0.25 mg/L; AZI 1 mg/L (both R by EUCAST)
- Outbreak of HL-AZI-R gonorrhoea
  - MICs, >256 mg/L (not a formal criterion)

Fifer et al. NEJM 2016; 374: 2504-6

Public Health England

Defence : Better Surveillance

33

Spotlight graphic: courtesy Tracey Guise, BSAC

Public Health England

The complexities of AMR

Antimicrobial Usage
All sectors

Patients, non-human reservoirs
Hospital / community setting;
risk factors; outcomes

Host species
Strains, clones

Genes
etc.

34 Webber Training Teleclass, 10th April 2018 © Crown Copyright

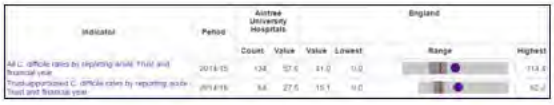
Public Health England

Monitoring antibiotic usage in England (ESPAUR)

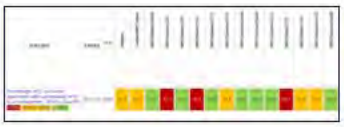
- Established by PHE in 2013 in response to the strategy
- Focuses on bringing together NHS, PHE, Private sector across all prescribers and clinicians to improve
  - Surveillance data on antibiotic resistance and prescribing
  - Antimicrobial stewardship activities
  - Education and training for healthcare professionals
  - Education and awareness to public

35 Webber Training Teleclass, 10th April 2018 © Crown Copyright

Public Health England



Open access to surveillance data

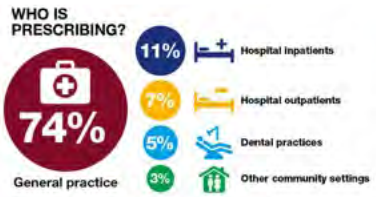


- Fingertips: http://fingertips.phe.org.uk/
- AMR local indicators hosted on PHE fingertips site contain a selection of data across 5 domains:
  - Antimicrobial Resistance
  - Antibiotic Prescribing
  - Healthcare Associated Infection
  - Infection Prevention and Control
  - Antimicrobial Stewardship
- Indicators are intended as information for action and may enable healthcare organisations to **benchmark** the data for their organisation

36 Webber Training Teleclass, 10th April 2018 © Crown Copyright

Public Health England

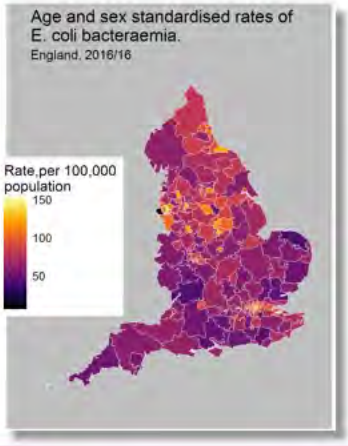
Simple messages …for targeting action



37 Webber Training Teleclass, 10th April 2018 © Crown Copyright

Public Health England

…and more questions to challenge us



- Regional variations in E. coli BSI rates
- Why ?
- Socio-economic deprivation scores and other indices ?
- Intervention measures

38 Webber Training Teleclass, 10th April 2018 © Crown Copyright

Courtesy: Alan Johnson & Susan Hopkins, PHE

Public Health England

We need to build global capacity

39 Webber Training Teleclass, 10th April 2018 © Crown Copyright

Public Health England

AMR surveillance in Africa

- no recent (>2013) AMR data published for >40% of countries on the continent and only a few of those were surveillance data.
- high level of resistance to commonly prescribed antibiotics in all regions:
  - trimethoprim (MR: 33.9%–100%), ampicillin (MR: 7.9%–100%) and penicillin (MR: 0%–75%)
- the standardization and quality of microbiological data must be improved.
  - unverified reports of highly unusual resistance patterns […], such as penicillin-resistant *S. pyogenes* and vancomycin-resistant *S. aureus*.

40 Webber Training Teleclass, 10th April 2018 © Crown Copyright Tadesse *et al. BMC Infect Dis* 2017; 17: 616

Public Health England

Defence : Alert Reporting

"Everything *more resistant* than everything else"

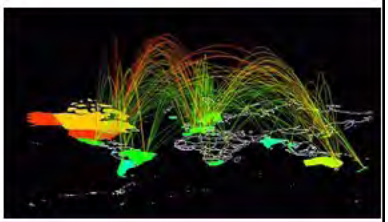
41

Spotlight graphic: courtesy Tracey Guise, BSAC

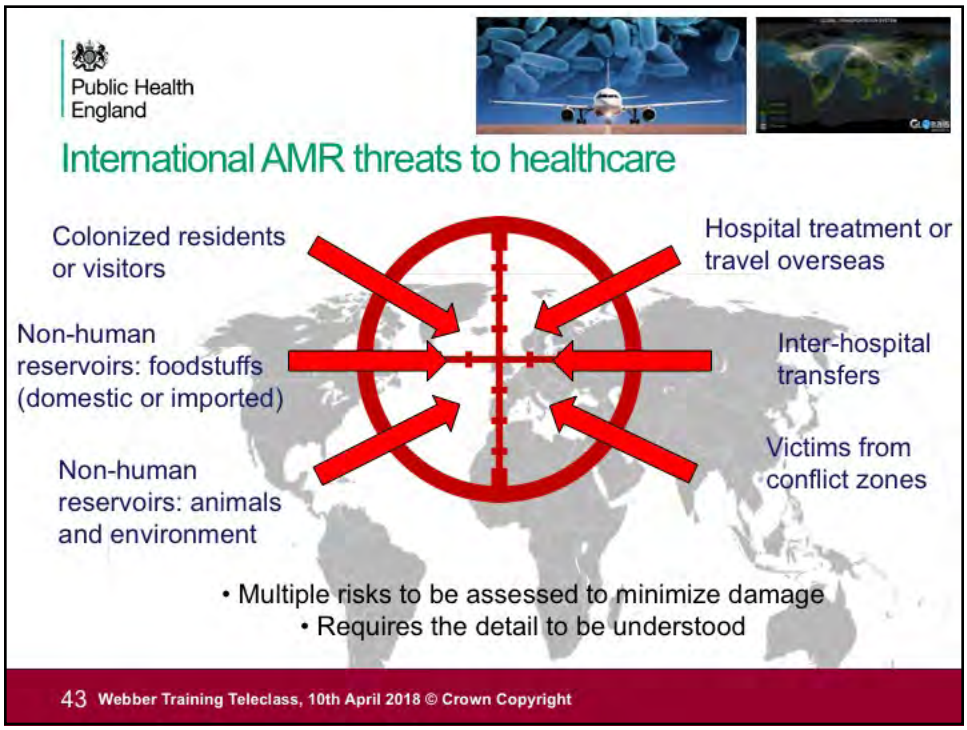
Public Health England

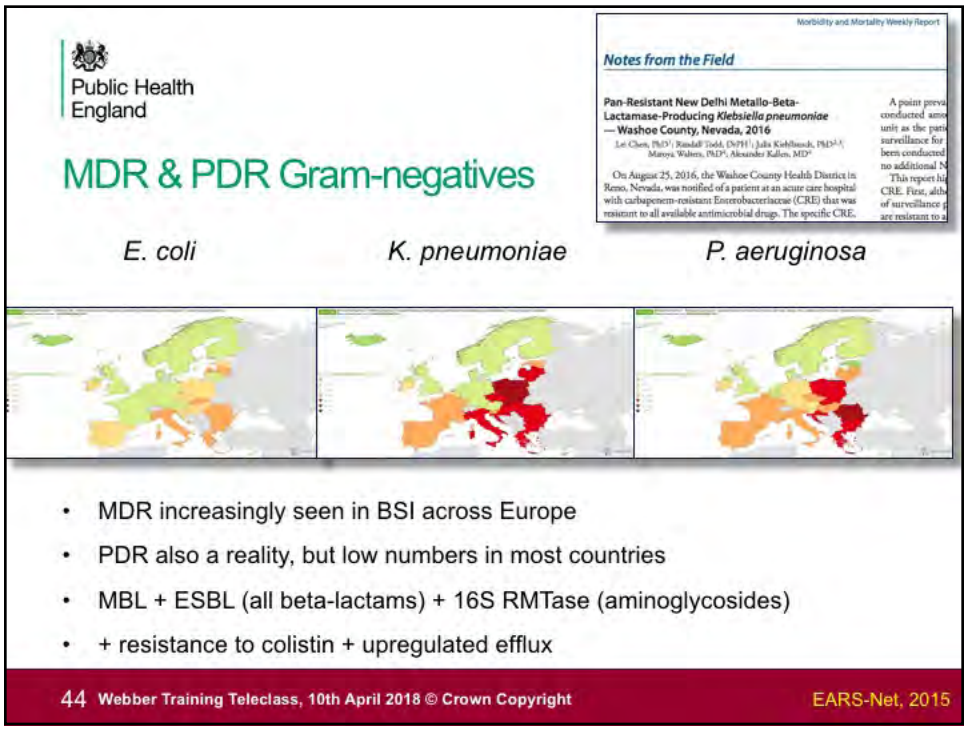
National & international capacity building

- Without lab testing we're blind to (the extent of) AMR problems
- Improve lab access; aim for a reference lab in every country / region
  - Each serving as the hub of a national network
  - Each acting as a spoke in an international network
  - Performing essential techniques, proficient to international standards
  - Sharing data / experience



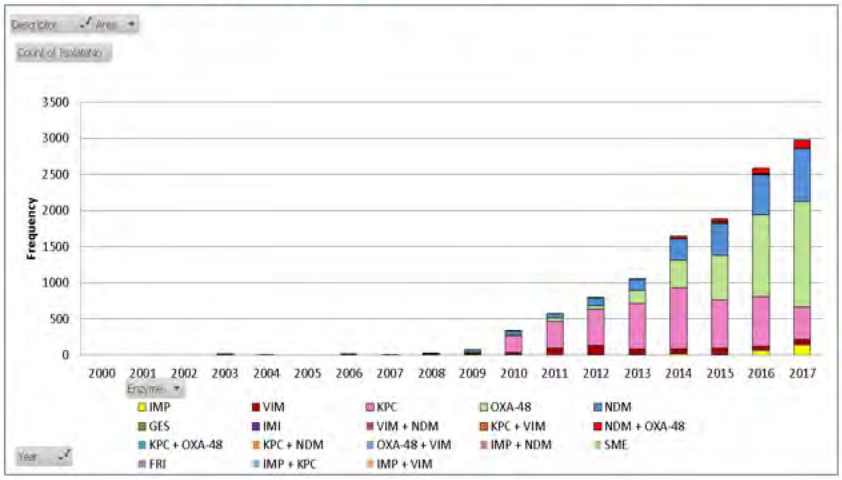
42 Webber Training Teleclass, 10th April 2018 © Crown Copyright


Public Health England
International AMR threats to healthcare
Colonized residents or visitors
Hospital treatment or travel overseas
Non-human reservoirs: foodstuffs (domestic or imported)
Inter-hospital transfers
Victims from conflict zones
Non-human reservoirs: animals and environment
• Multiple risks to be assessed to minimize damage
• Requires the detail to be understood
43 Webber Training Teleclass, 10th April 2018 © Crown Copyright


Public Health England
MDR & PDR Gram-negatives
Notes from the Field
Pan-Resistant New Delhi Metallo-Beta-Lactamase-Producing Klebsiella pneumoniae — Washoe County, Nevada, 2016
E. coli
K. pneumoniae
P. aeruginosa
• MDR increasingly seen in BSI across Europe
• PDR also a reality, but low numbers in most countries
• MBL + ESBL (all beta-lactams) + 16S RMTase (aminoglycosides)
• + resistance to colistin + upregulated efflux
44 Webber Training Teleclass, 10th April 2018 © Crown Copyright
EARS-Net, 2015

Public Health England

CPE in the UK, 2000-2017



45 Webber Training Teleclass, 10th April 2018 © Crown Copyright AMRHAI, Unpublished data

Public Health England

Fighting 'AMR' outbreaks is hugely expensive

46 Webber Training Teleclass, 10th April 2018 © Crown Copyright

Public Health England

Discovery of plasmidic colistin resistance; *mcr-1*

	Year	Positive isolates (%)/number of isolates
Escherichia coli		
Pigs at slaughter	All	166 (20·6%)/804
Pigs at slaughter	2012	31 (14·4%)/216
Pigs at slaughter	2013	68 (25·4%)/268
Pigs at slaughter	2014	67 (20·9%)/320
Retail meat	All	78 (14·9%)/523
Chicken	2011	10 (4·9%)/206
Pork	2011	3 (6·3%)/48
Chicken	2013	4 (25·0%)/16
Pork	2013	11 (22·9%)/48
Chicken	2014	21 (28·0%)/75
Pork	2014	29 (22·3%)/130
Inpatient	2014	13 (1·4%)/902
Klebsiella pneumoniae		
Inpatient	2014	3 (0·7%)/420

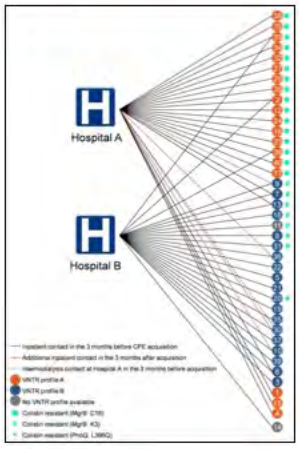
Table 2: Prevalence of colistin resistance gene *mcr-1* by origin

47 Webber Training Teleclass, 10th April 2018 © Crown Copyright

Liu et al. *Lancet Infect Dis.* 2015 Nov 18. pii: S1473-3099(15)00424-7

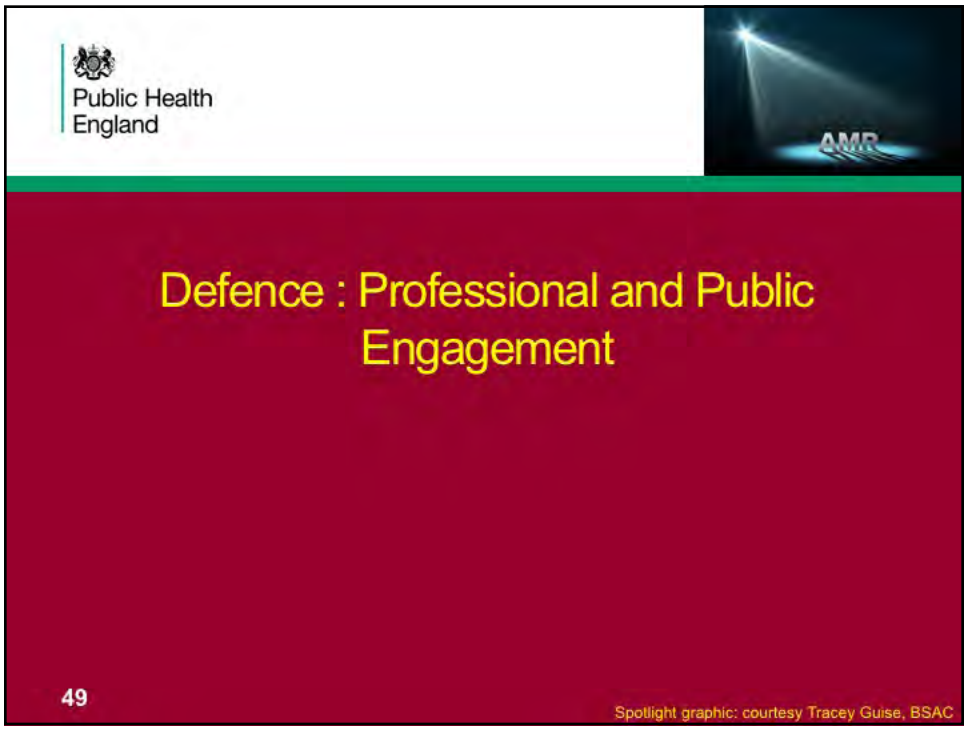
Public Health England

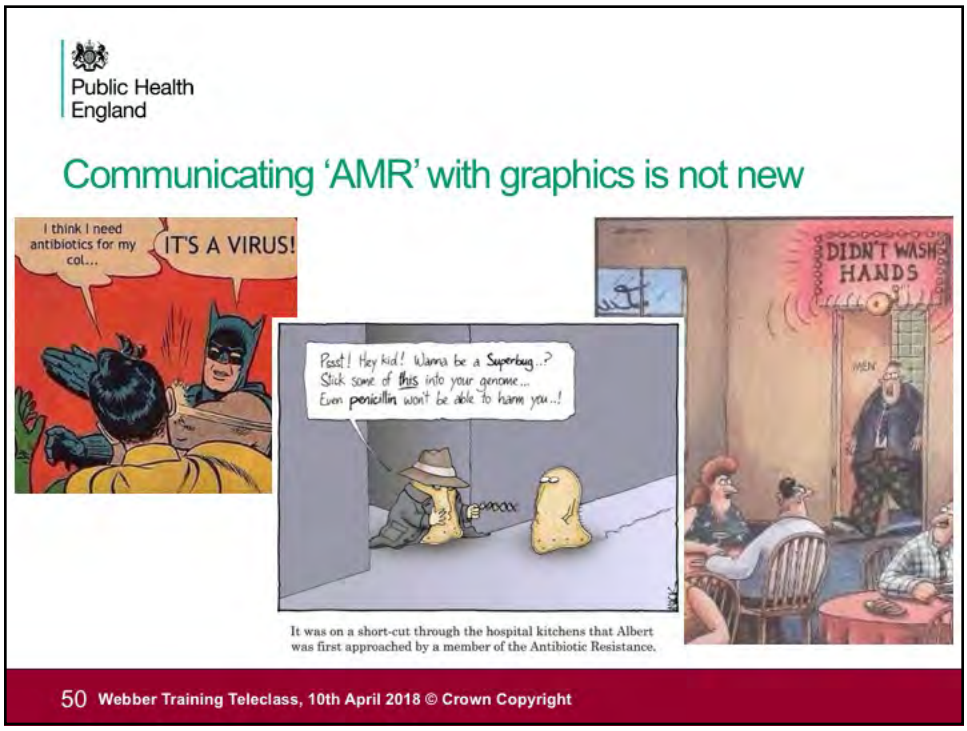
If focus is on *mcr* we may lose sight of other colistin resistance



48 Webber Training Teleclass, 10th April 2018 © Crown Copyright

Otter *et al. Sci Rep* 2017; 7(1):12711


Public Health England
AMR
Defence : Professional and Public Engagement
49
Spotlight graphic: courtesy Tracey Guise, BSAC

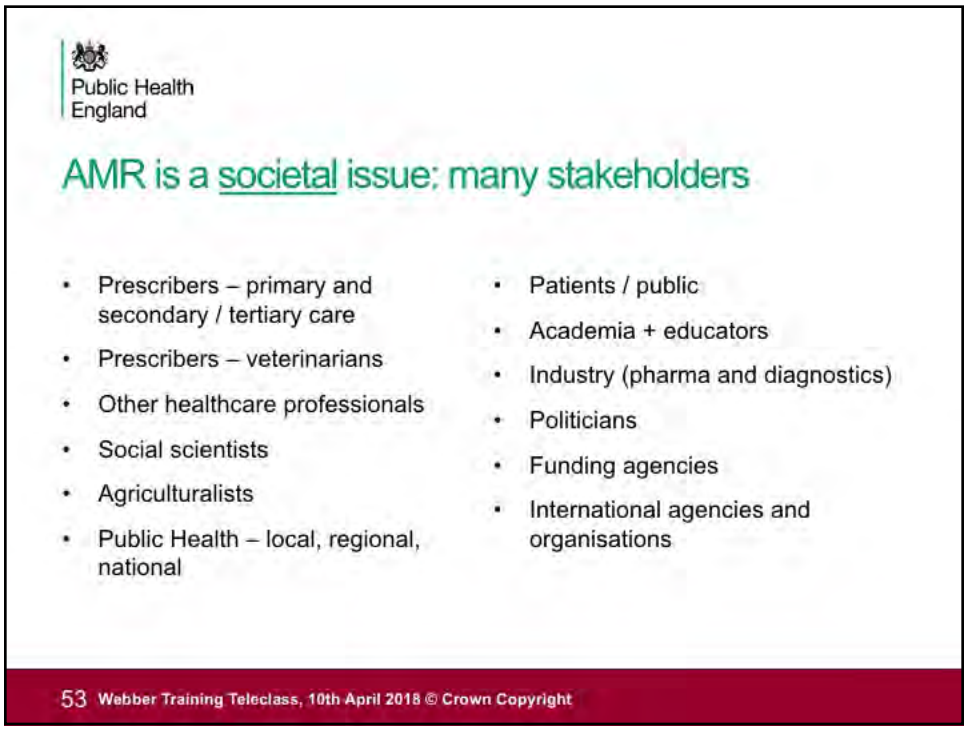

Public Health England
Communicating 'AMR' with graphics is not new
I think I need antibiotics for my col...
IT'S A VIRUS!
Psst! Hey kid! Wanna be a Superbug..? Stick some of this into your genome... Even penicillin won't be able to harm you..!
DIDN'T WASH HANDS
WHEN
It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.
50 Webber Training Teleclass, 10th April 2018 © Crown Copyright

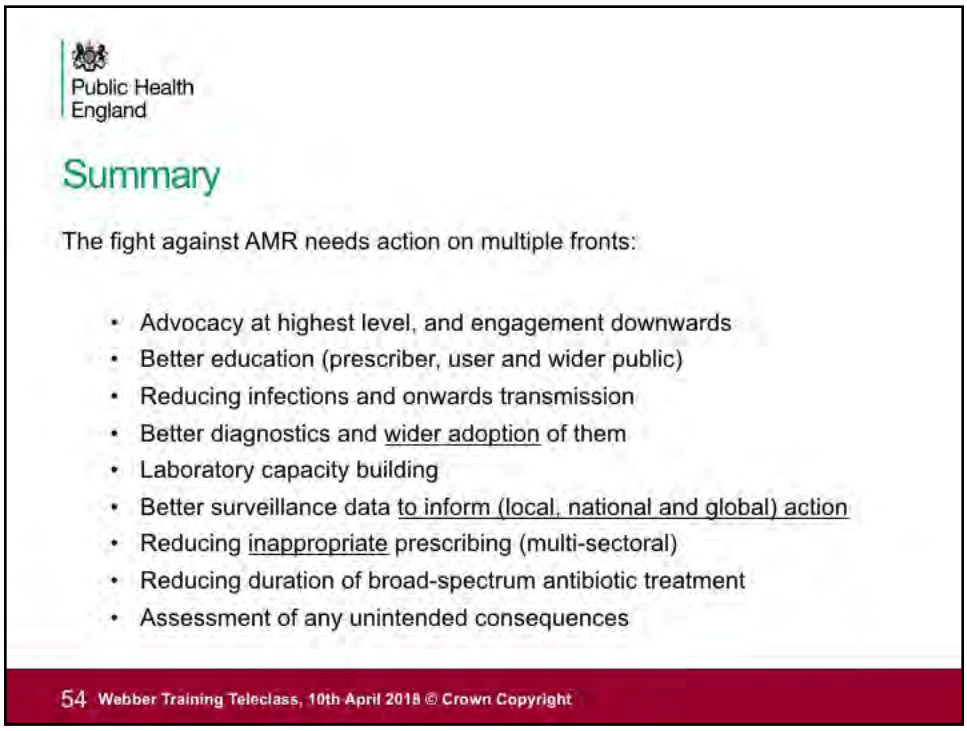
Public Health England

…, but is now mainstream and international

Public Health England

Groundbreaking UK engagement initiatives


Public Health England
AMR is a societal issue: many stakeholders
• Prescribers – primary and secondary / tertiary care
• Prescribers – veterinarians
• Other healthcare professionals
• Social scientists
• Agriculturalists
• Public Health – local, regional, national
• Patients / public
• Academia + educators
• Industry (pharma and diagnostics)
• Politicians
• Funding agencies
• International agencies and organisations
53 Webber Training Teleclass, 10th April 2018 © Crown Copyright


Public Health England
Summary
The fight against AMR needs action on multiple fronts:
• Advocacy at highest level, and engagement downwards
• Better education (prescriber, user and wider public)
• Reducing infections and onwards transmission
• Better diagnostics and wider adoption of them
• Laboratory capacity building
• Better surveillance data to inform (local, national and global) action
• Reducing inappropriate prescribing (multi-sectoral)
• Reducing duration of broad-spectrum antibiotic treatment
• Assessment of any unintended consequences
54 Webber Training Teleclass, 10th April 2018 © Crown Copyright

Hopes, Hypes and Multivallate Defences Against Antimicrobial Resistance
Professor Neil Woodford, Public Health England
Denver Russell Memorial Teleclass

www.webbertraining.com/schedulep1.php	
April 12, 2018	UNDERSTANDING RISK PERCEPTIONS AND RESPONSES OF THE PUBLIC, HEALTHCARE PROFESSIONALS, AND THE MEDIA: THE CASE FOR *CLOSTRIDIUM DIFFICILE* Speaker: **Dr. Emma Burnett**, University of Dundee, Scotland
April 18, 2018	*(South Pacific Teleclass)* GENETIC SIMILARITIES BETWEEN ORGANISMS ISOLATED FROM THE ICU Speaker: **Prof. Slade Jenson**, Western Sydney University, Australia
April 19, 2018	TOPICAL ANTIBIOTICS TO PREVENT POST-OPERATIVE SURGICAL INFECTION ... IS THE PARADIGM CHANGING? Speaker: **Dr. Hilary Humphreys**, The Royal College of Surgeons in Ireland
May 3, 2018	*(FREE ... WHO Teleclass - Europe)* SPECIAL LECTURE FOR 5 MAY Speaker: **Prof. Didier Pittet**, University of Geneva Hospitals
May 10, 2018	*(FREE CBIC Teleclass)* HOW THE CERTIFICATION BOARD OF INFECTION CONTROL (CBIC) WORKS FOR YOU Speaker: **To be announced**
May 17, 2018	THE SILENT TSUNAMI OF AZOLE-RESISTANCE IN THE OPPORTUNISTIC FUNGUS *ASPERGILLUS FUMIGATUS* Speaker: **Prof. Paul E. Verweij**, Radboud University Center of Expertise in

Thanks to Teleclass Education

PATRON SPONSORS

Diversey — www.diversey.com

VIROX — www.virox.com

GOJO — www.gojo.com

World Health Organization — Infection Prevention and Control Global Unit — www.who.int/gpsc/en

A Webber Training Teleclass
Hosted by Prof. Jean-Yves Maillard, Cardiff University, Wales
www.webbertraining.com