Antimicrobial Resistance and Stewardship: a national picture

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CDDFT

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11 March 2013 Last updated at 13:36

Antibiotics resistance 'as big ... terrorism' - medical chief

COMMENTS (1034)

By Fergus Walsh
Medical correspondent

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NEWS

Antibiotic resistance: World on cusp of 'post-antibiotic era'

By James Gallagher
Health editor, BBC News website

13 November 2015 | Health

The world is on the cusp of a "post-antibiotic era", scientists have warned after finding bacteria resistant to drugs used when all other treatments have failed.

They identified bacteria able to shrug off the drug of last resort - colistin - in patients and livestock in China.

They said that resistance would spread around the world and raised the spectre of untreatable infections.

Experts said the worrying development needed to act as a global wake-up call.

Bacteria becoming completely resistant to treatment - also known as **the antibiotic apocalypse** - could plunge medicine back into the dark ages.

Common infections would kill once again, while surgery and cancer therapies, which are reliant on antibiotics, would be under threat.

theguardian

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...3 January 2013 19.41 GMT

...t know antibiotic-resistant ... gonorrhea and TB that

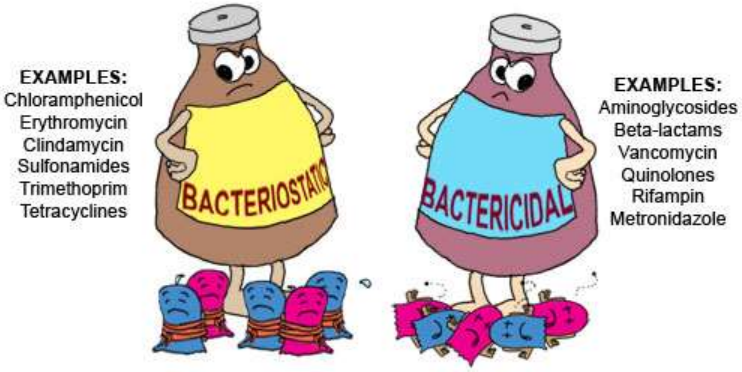
... warned MPs that the rise in ... national emergency comparable ...

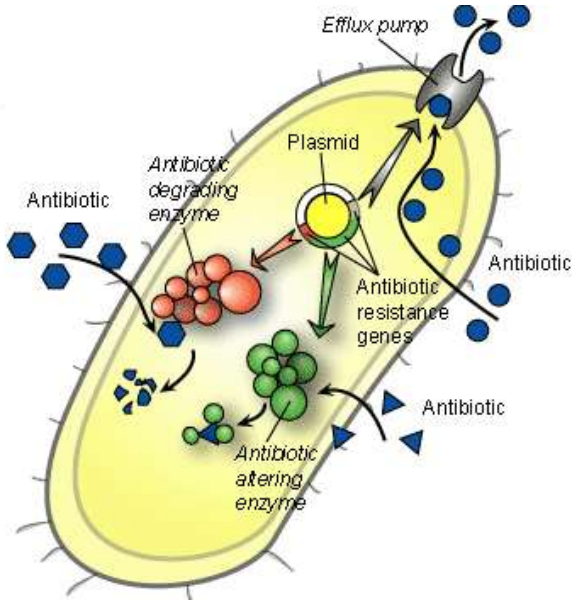
NHS England

www.england.nhs.uk

What is antimicrobial resistance?

- Antibacterials either kill or stop bacteria replicating
- Bacteria try to avoid being killed in 4 ways
- Can mutate (<1 day) or inherit resistance.
- Can spread their resistance mechanisms to other species (on plasmids), and then onto other people.

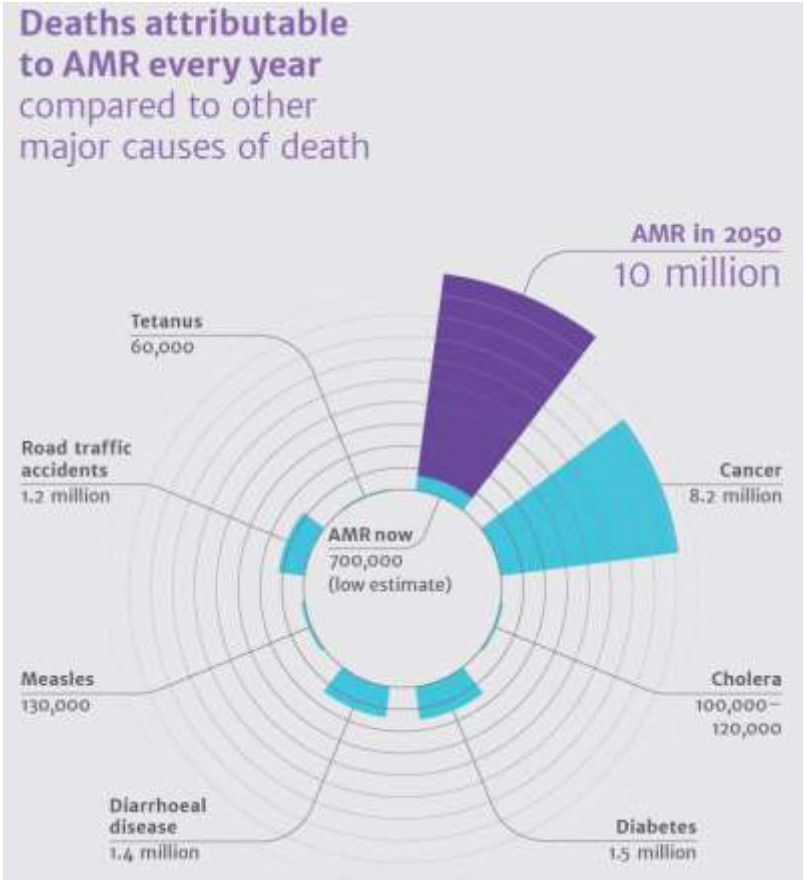


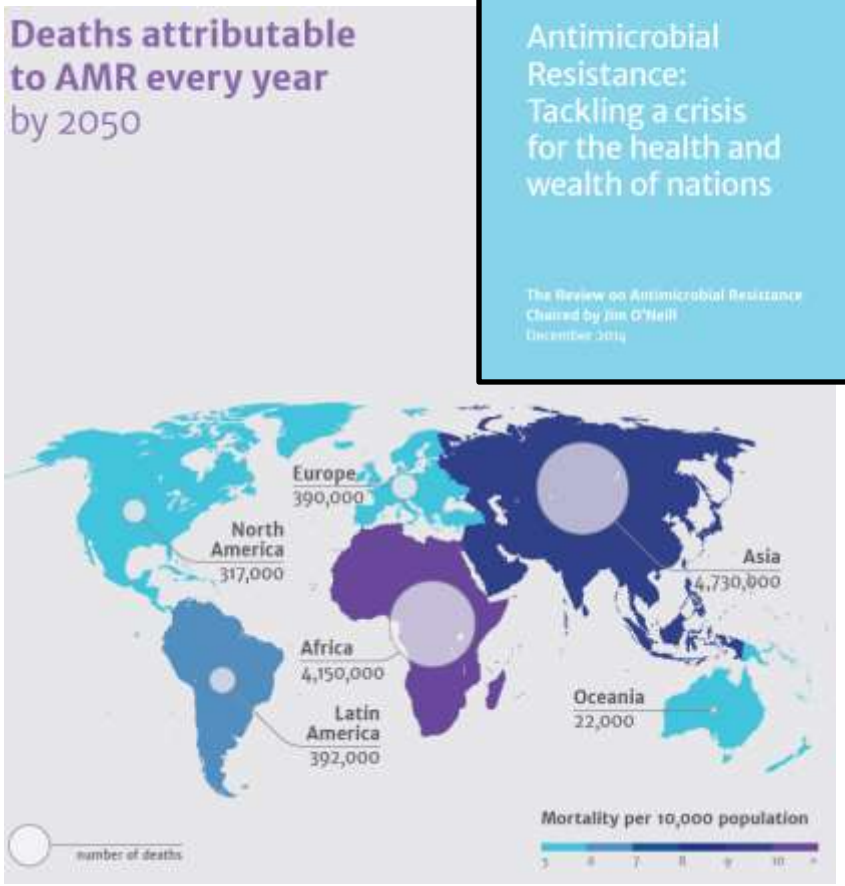


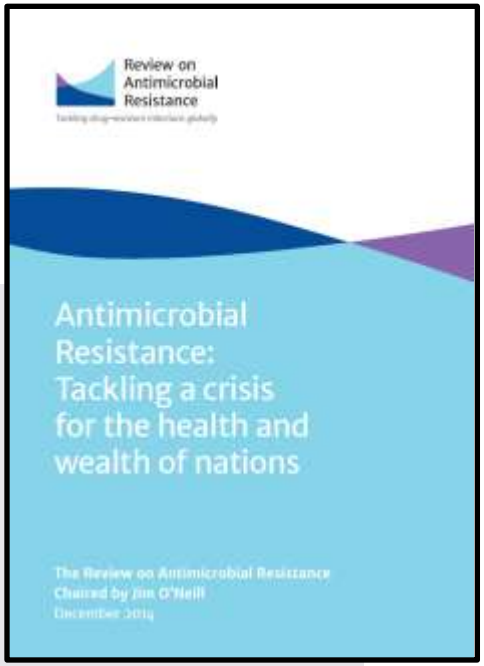
Inappropriate Antimicrobial Use

- Risks to patients
  - Resistant infections
  - Healthcare-associated infections (HCAIs)
    - *Clostridium difficile*
    - MRSA
    - Others
- Financial cost
  - Cost of inappropriate antibiotics
  - Cost of treating resistant infections/HCAIs

The future – Jim O'Neil







No (clean-contaminated/dirty) surgery, no chemotherapy (neutropenic sepsis)
Cost will be $100 trillion per year ($100,000,000,000,000)

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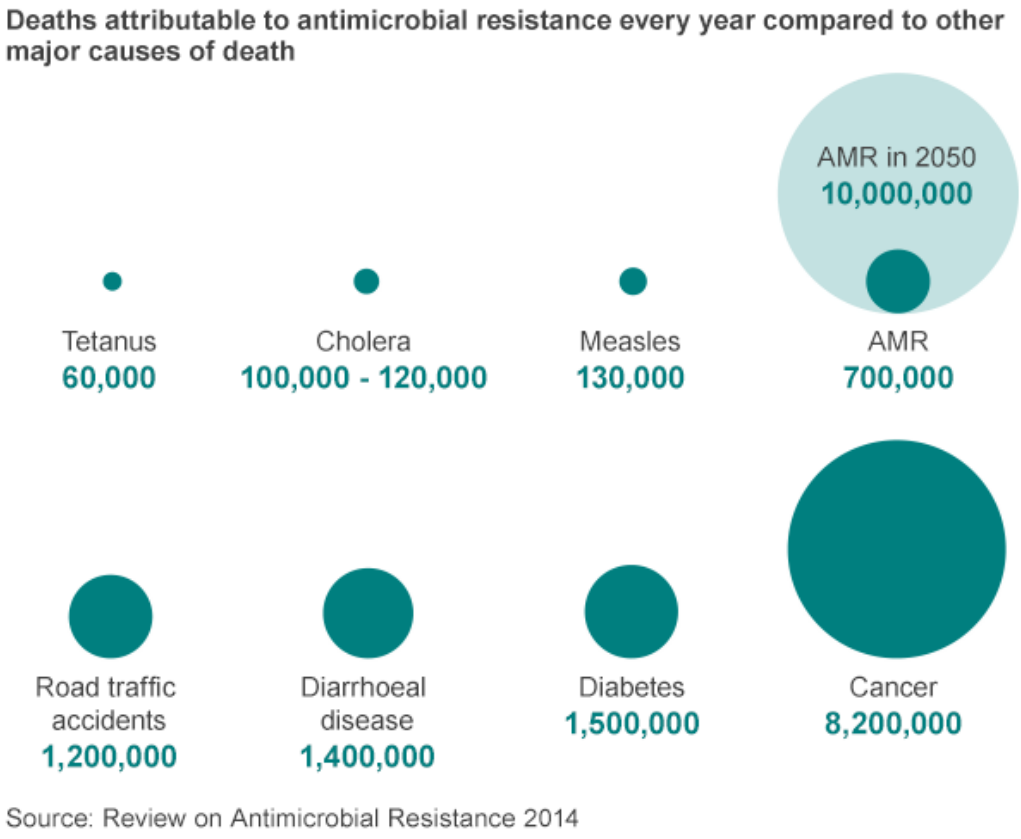
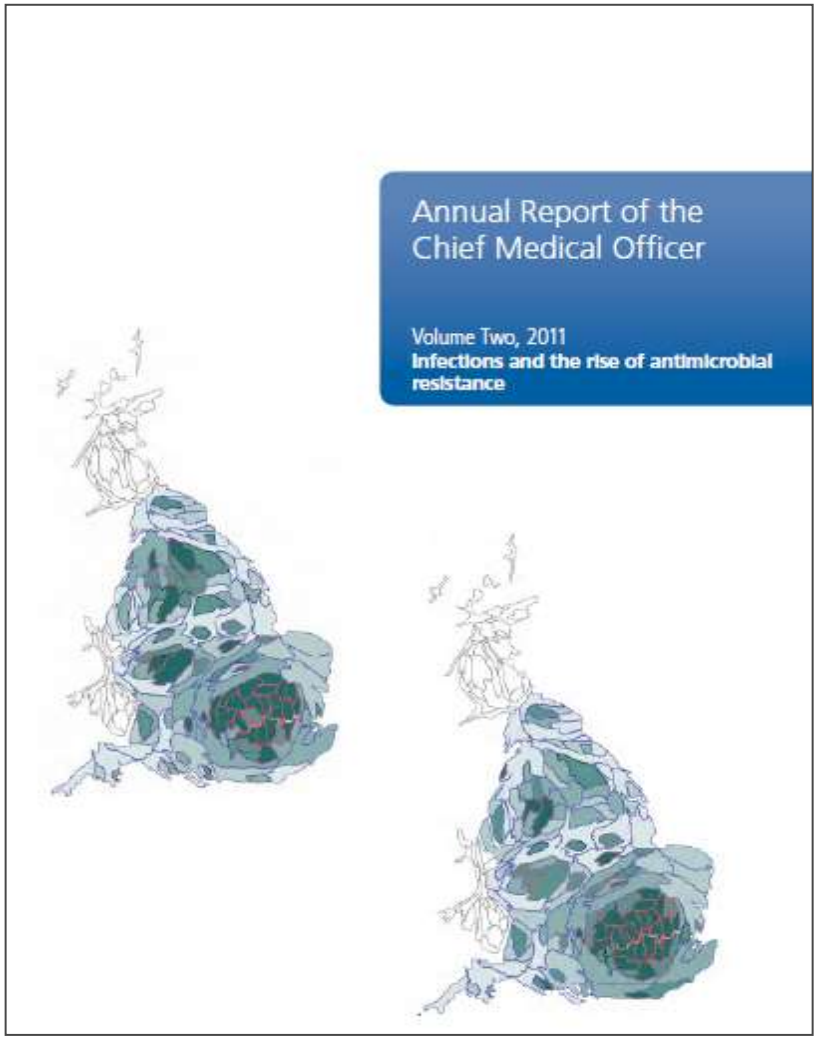
Superbugs to kill 'more than cancer' by 2050

NHS England

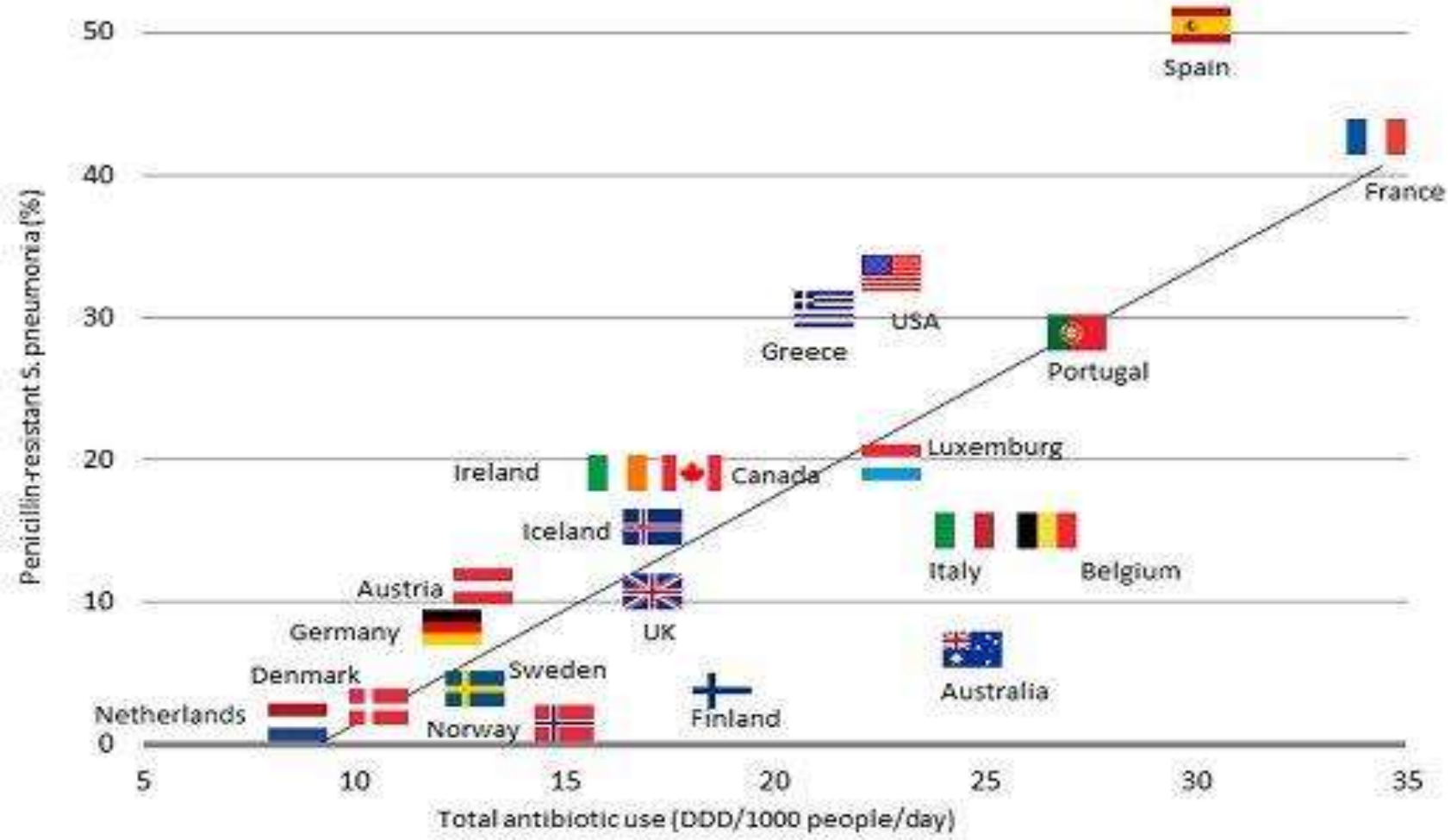


CMO Report



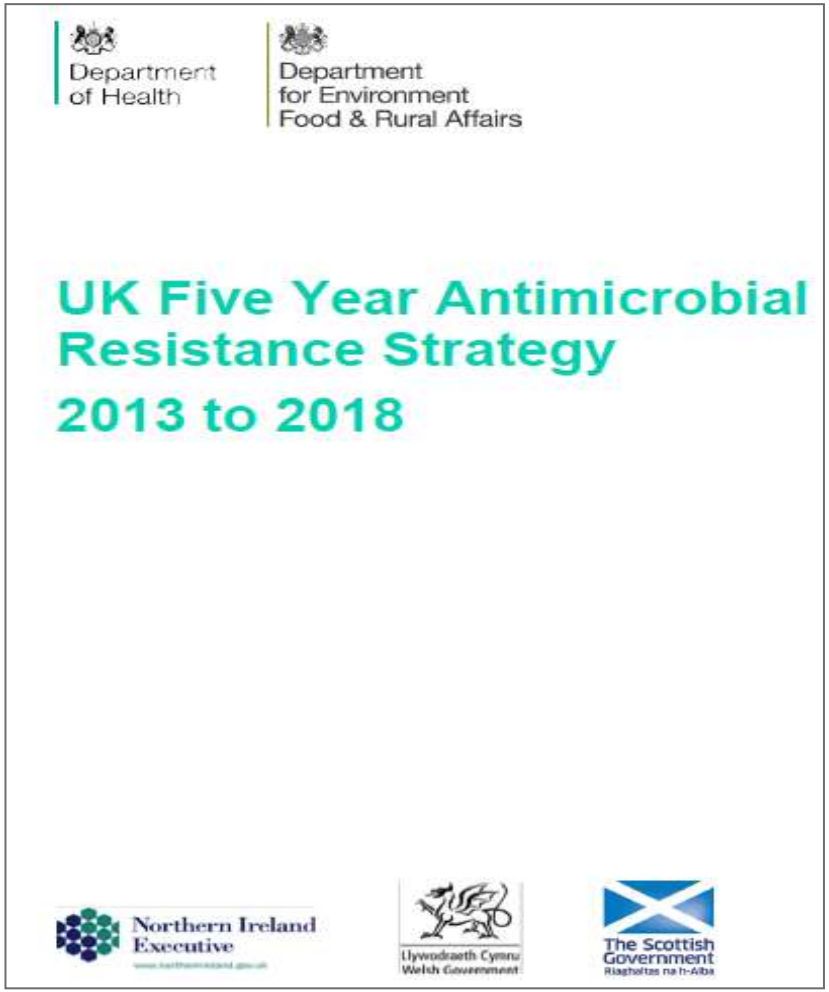
- Existing evidence clearly shows that as more antibiotics are used, selection of resistant organisms occurs.
- Paucity of new antimicrobials being developed.
- Conserve and make more effective use of our existing antibiotics
- Improved clinical practice will require changes in attitudes, behaviours and beliefs about antibiotics
- National risk register

G7 Health Ministers meeting Oct 2015
Antibiotic consumption links to AMR



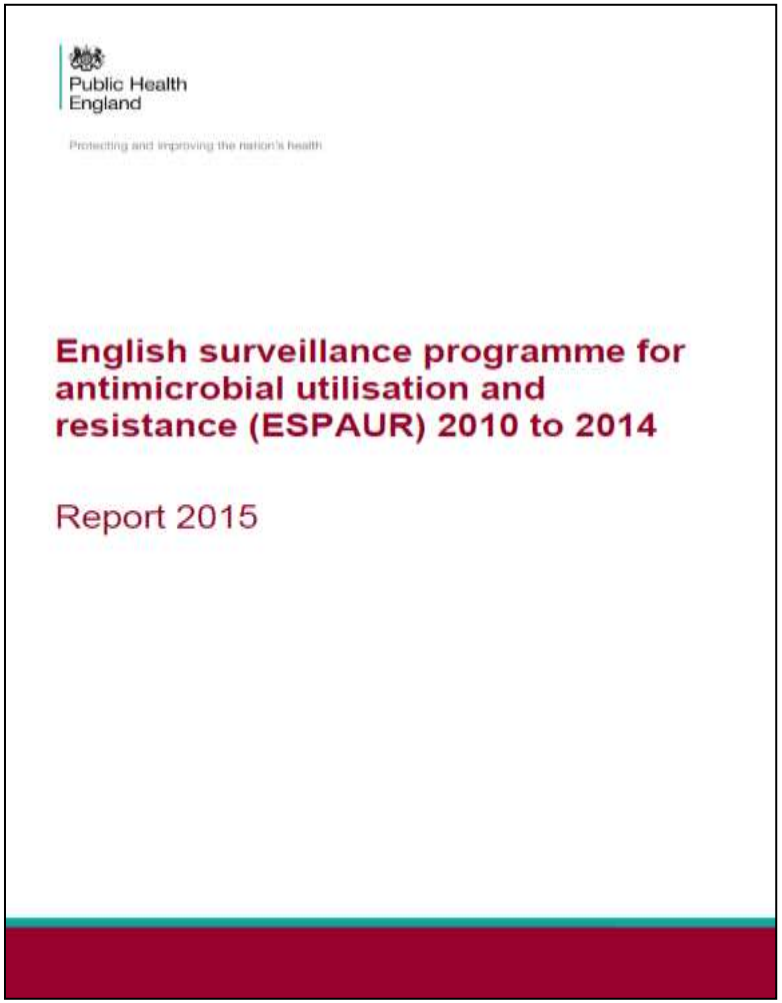
7 Key Areas

- Improving infection prevention and control practices
- Optimising prescribing practice
- Improving professional education, training and public engagement
- Developing new drugs, treatments and diagnostics
- Better access to and use of surveillance data
- Better identification and prioritisation of AMR research needs
- Strengthened international collaboration



ESPAUR 2015

- Antimicrobial
  - Resistance
  - Consumption
  - Stewardship



Antimicrobial Resistance

- The number of patients with bloodstream infections has increased each year from 2010 to 2014
  - *E. coli* increased by 15.6%
  - *K. pneumoniae* increased by 20.8%
- *S. pneumoniae* declined by 25% - likely due to introduction of new pneumococcal vaccine in 2010

NHS England

Table 0.1 Antibiotic resistance in key infections, England, 2010–2014

Bacteria	Antibiotic resistance (non-susceptibility) metric	Proportion resistant in 2014 (%)	2014 compared to 2010*
Bloodstream infections			
Escherichia coli	% NS to ciprofloxacin	18.7	↔
E. coli	% NS to cefotaxime and/or ceftazidime	11.1	↑
E. coli	% NS to gentamicin	9.6	↔
E. coli	% NS to imipenem and/or meropenem	0.1	↔
E. coli	% NS to co-amoxiclav	42.0	↑
E. coli	% NS to piperacillin/tazobactam	11.0	↑
Klebsiella pneumoniae	% NS to ciprofloxacin	10.9	↔
K. pneumoniae	% NS to cefotaxime and/or ceftazidime	12.1	↑
K. pneumoniae	% NS to gentamicin	7.5	↔
K. pneumoniae	% NS to imipenem and/or meropenem	1.5	↑
K. pneumoniae	% NS to piperacillin/tazobactam	16.9	↑
Pseudomonas spp.	% NS to ceftazidime	7.4	↔
Pseudomonas spp.	% NS to imipenem and/or meropenem	11.5	↔
Streptococcus pneumoniae	% NS to penicillin	4.2	↔
Enterococcus spp.	% NS to vancomycin	14.2	↑
Staphylococcus aureus	% NS to methicillin	10.0	↓
Acinetobacter spp	% NS to colistin	3.5	↔

ESPAUR 2015

Antimicrobial Consumption 2010-2014 (DDD per 1000 inhabitants)

- Antibiotic consumption has increased in England by a total of 6.5%
  - General Practice increased 6.2%
  - Hospital inpatients increased by 11.7%
  - Other community prescriptions (e.g dentists) increased by 5.5%

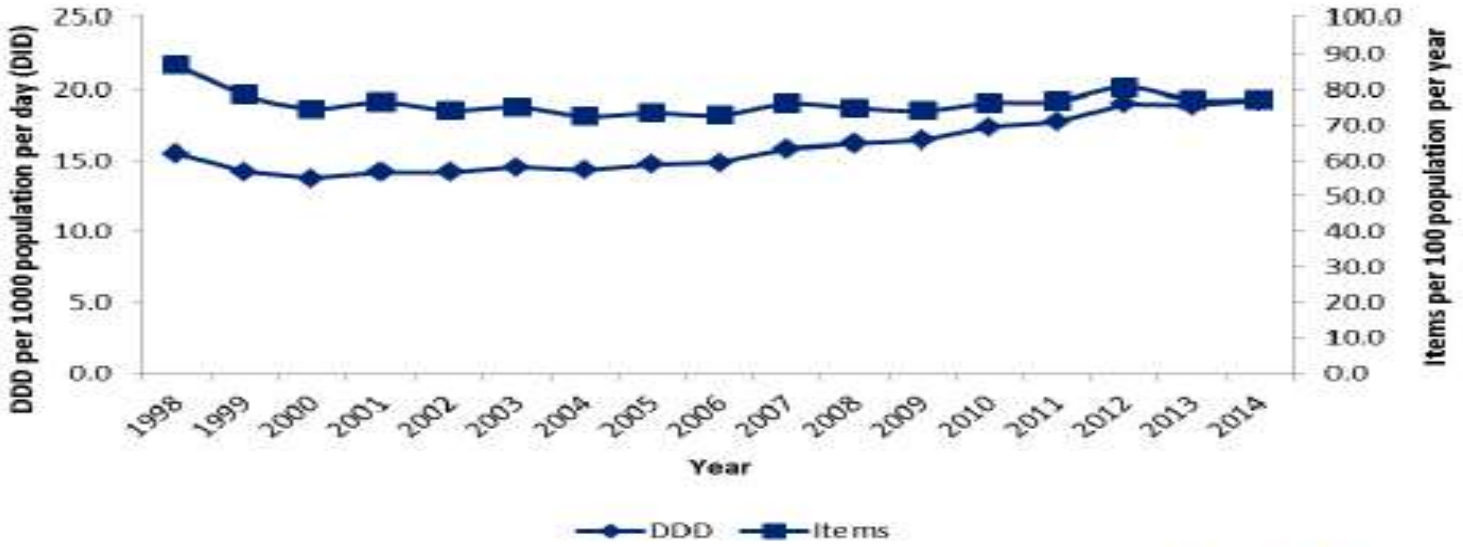


Figure 3.1 Prescriptions dispensed in the community, expressed as DDD per 1000 inhabitants per day and items per 100 inhabitants per year, England, 1998–2014

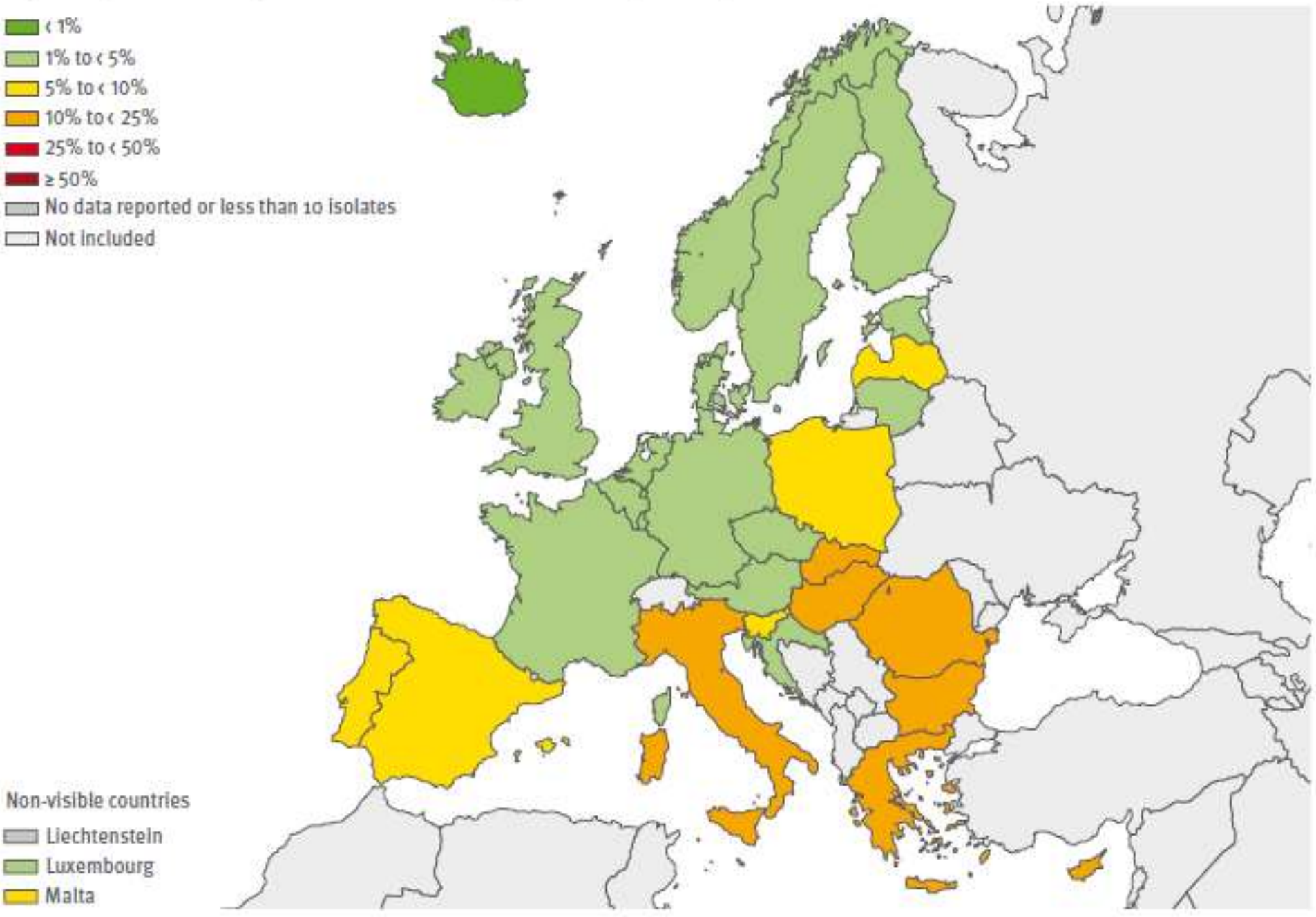
ESBL's

- Extended Spectrum β-lactamases
- Associated with Gram negative bacteria
  - Poorer clinical outcomes
  - Increased mortality rates
- Increasing prevalence within the community
- Multi-drug resistant

Antibiotic treatment ESBL

- Benzylpenicillin
- Ertapenem
- Gentamicin
- Levofloxacin
- Co-amoxiclav
- Teicoplanin
- Ceftriaxone
- Meropenem
- Daptomycin
- Flucloxacillin
- Ciprofloxacin
- Ceftazidime
- Linezolid
- Nitrofurantoin
- Colomycin
- Tigecycline
- Amikacin
- Amoxicillin
- Cefotaxime
- Fosfomycin
- Clarithromycin
- Clindamycin
- Chloramphenicol
- Cefuroxime
- Tazocin
- Vancomycin
- Co-trimoxazole
- Metronidazole
- Trimethoprim
- Gentamicin
- Pivmecillinam

Figure 3.4. ***Escherichia coli.*** **Percentage (%) of invasive isolates with combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides, by country, EU/ EEA countries, 2012**



Has 36%↑ in carbapenems driven AMR?

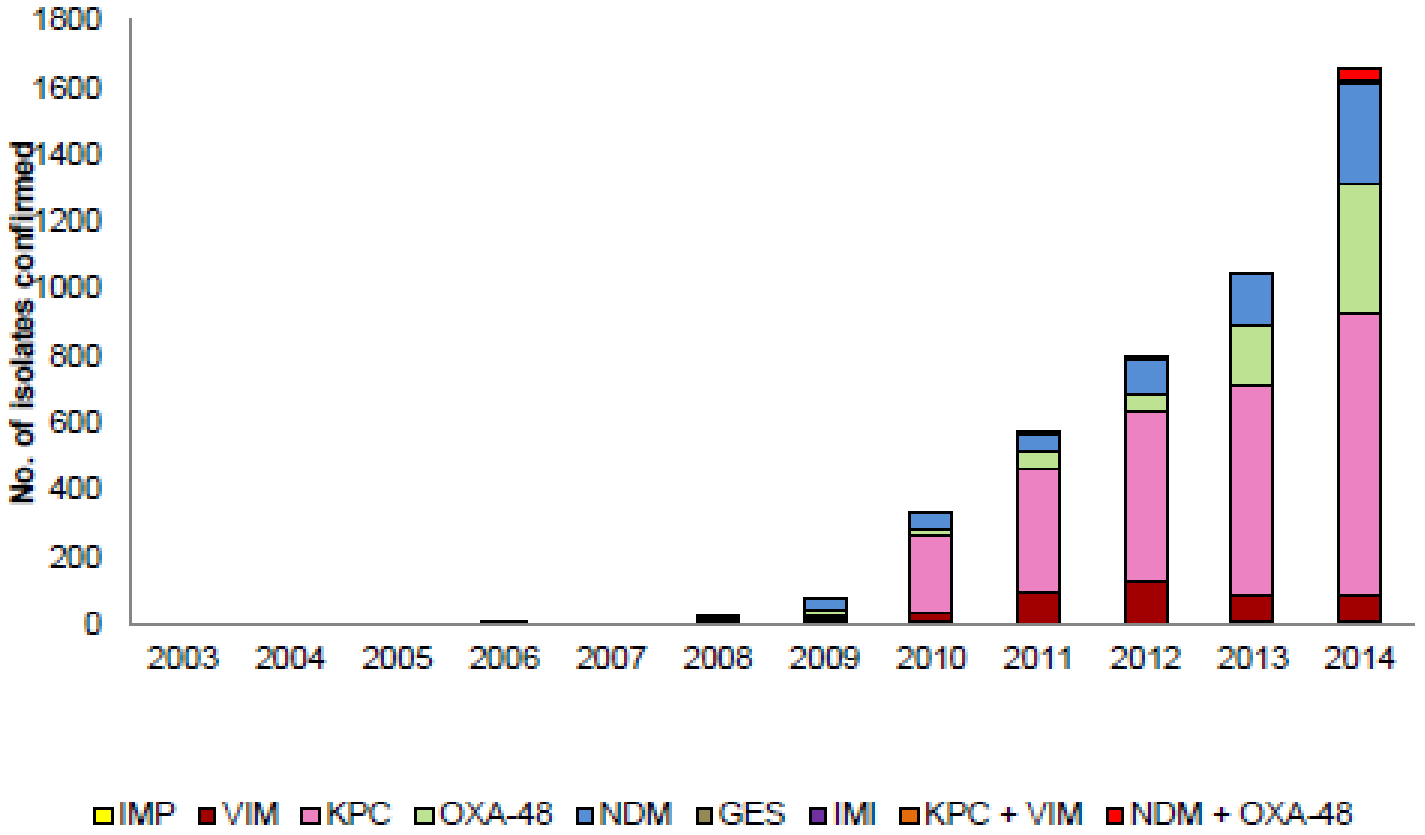


Figure 2.10 Number of isolates referred from UK hospital microbiology laboratories confirmed as carbapenemase-producing Enterobacteriaceae by AMRHAI, 2003–2014

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Manchester ↓ by 7% over 4 years

Table 1. Antibiotic susceptibilities of carbapenemase-producing Enterobacteriaceae isolates from the UK, submitted to the AMRHAI Reference Unit in 2014

Antibiotic	Proportion of susceptibility, % [a]					
	Metallo-enzyme producers (NDM, VIM, IMP) (n=c. 400)			Non-metallo-enzyme producers (KPC, OXA-48, GES, IMI) (n=c. 1250)		
	E. coli	*Klebsiella*	*Enterobacter / Citrobacter*	*E. coli*	*Klebsiella*	*Enterobacter / Citrobacter*
Imipenem (IPM)	3	2	3	48	7	40
IPM-EDTA [b]	100	88	94	69	17	42
Meropenem	6	5	8	73	12	51
Ertapenem	3	0	3	4	0	1
Ampicillin	0	0	0	0	0	0
Co-amoxiclav	1	0	0	1	0	0
Piperacillin (PIP)	0	0	1	0	0	1
PIP-tazobactam	2	0	1	1	0	1
Cefotaxime	1	0	0	10	3	13
Ceftazidime	1	0	0	25	7	34
Aztreonam	13	13	23	15	7	34
Ciprofloxacin	17	6	20	61	30	68
Gentamicin	31	24	24	51	56	66
Tobramycin	22	7	8	51	47	59
Amikacin	49	33	62	92	82	96
Colistin	100	93	93	100	94	100
Tigecycline	99	52	73	98	59	80

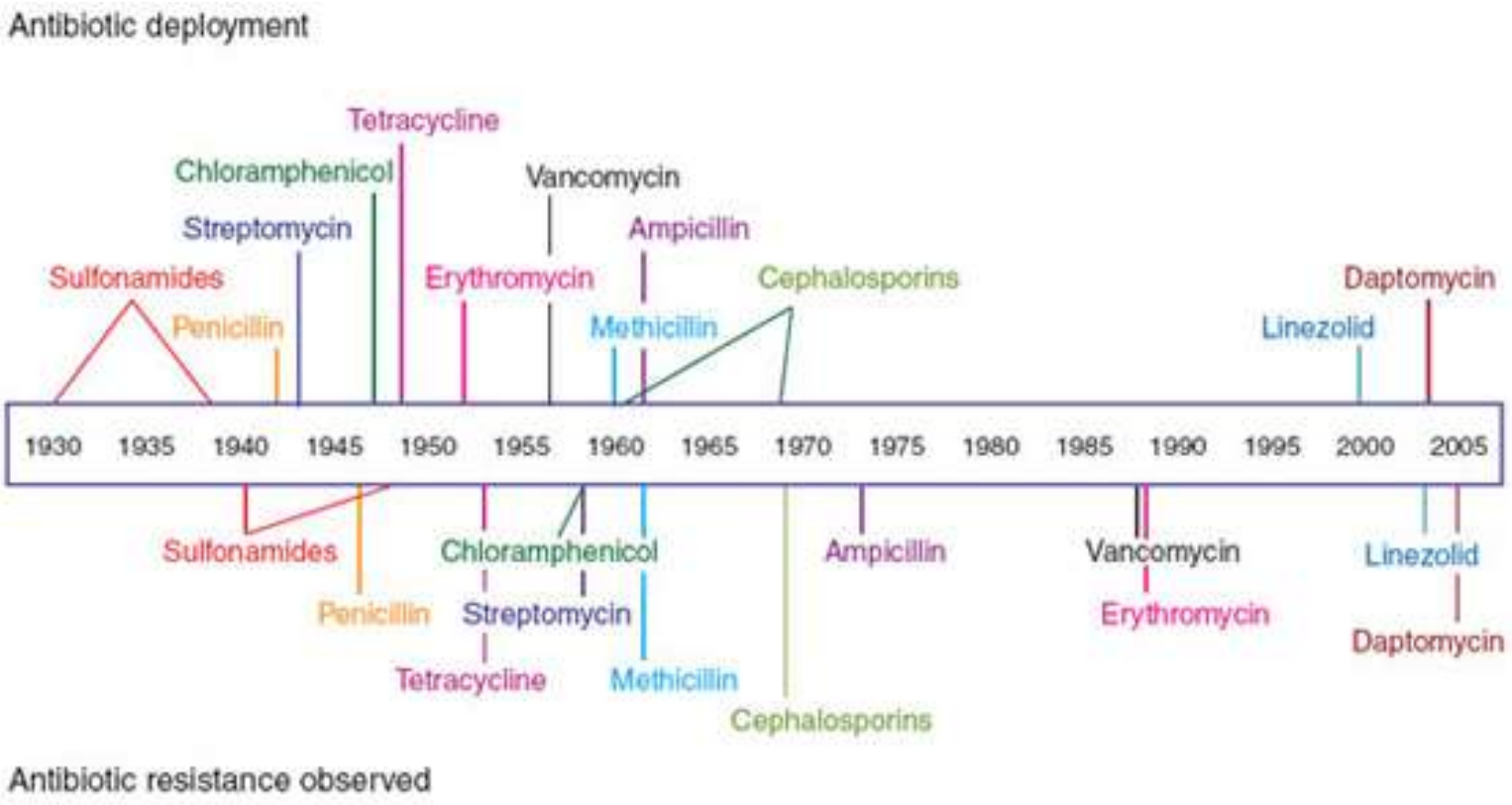
a. Susceptibility defined using BSAC v. 13 (June 2014) breakpoints

b. Diagnostic test to distinguish metallo- from non-metallo- enzymes; not for therapeutic use

Active in vitro against <50% isolates
Active in vitro against 50-90% isolates
Active in vitro against >90% isolates

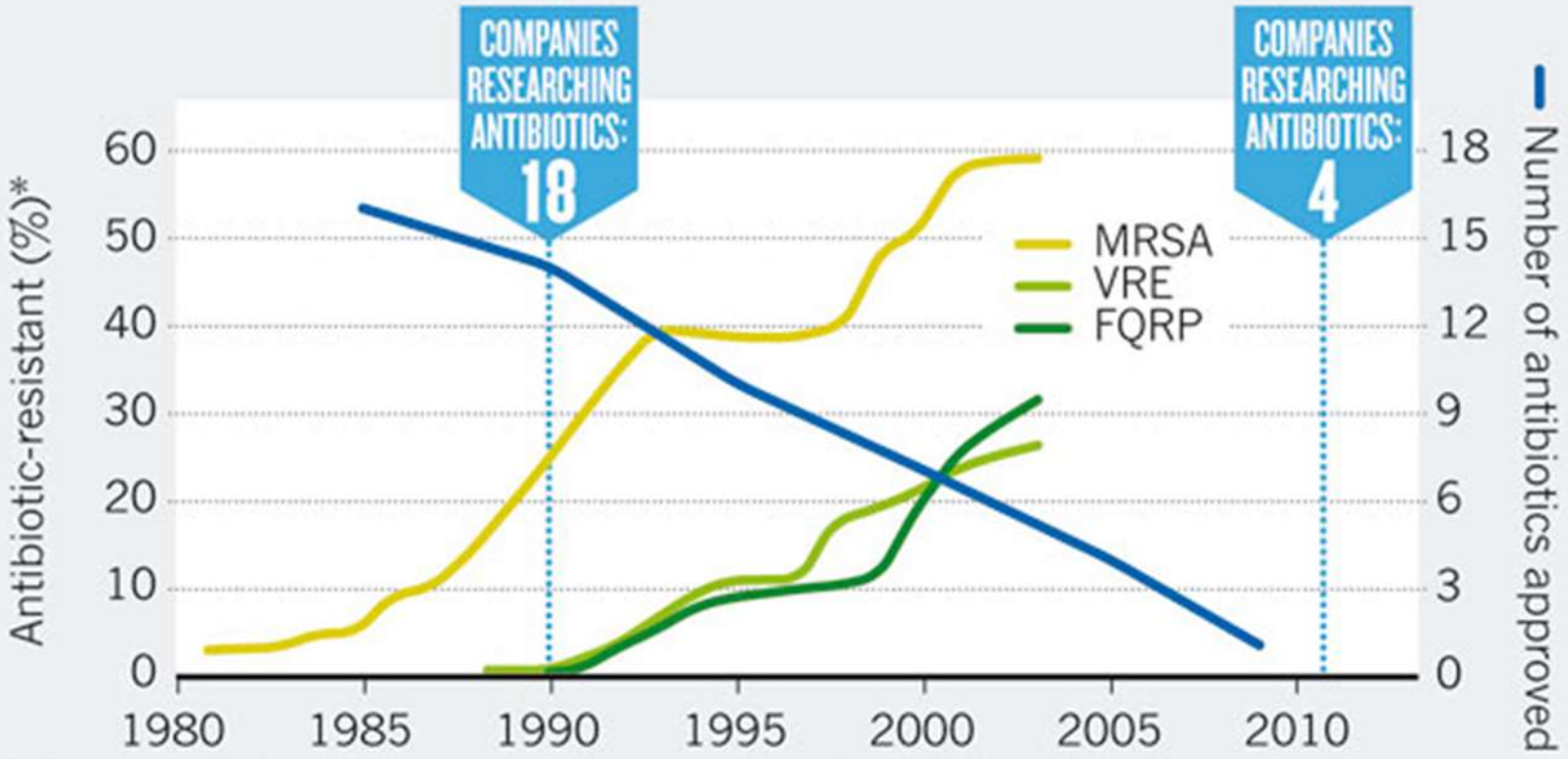
Public Health England
Infection report
Volume 9 Number 2 Published on: 16 January 2015

Why we need new antibiotics



A PERFECT STORM

As bacterial infections grow more resistant to antibiotics, companies are pulling out of antibiotics research and fewer new antibiotics are being approved.



*Proportion of clinical isolates that are resistant to antibiotic. MRSA, methicillin-resistant *Staphylococcus aureus*. VRE, vancomycin-resistant *Enterococcus*. FQRP, fluoroquinolone-resistant *Pseudomonas aeruginosa*.

Antibacterials are used for short courses = poor return on investment.
Registration requires trials in infections where unlikely to use
We reserve or don't use new ones. Eg ceftaroline: "it's a cephalosporin!"

New antibiotics

- Oritavancin IV weekly (Q2 ‘15) - cSSTI
- Telavancin IV daily G+ve HAP (Q3 ‘14) = teicoplanin / vancomycin
- Dalbavancin IV weekly – cSSTI (Q1 ’15), CAP 2017
- Tedizolid –po/IV daily - Q2’15: like linezolid but without the interactions or haematological side-effects
- Ceftolozane-tazobactam IV – Q4’15: cUTI, cIAI (abdo), (VAP later) – covers ESBL E.coli and MDR PsA, but not Kleb pneum
- Ceftibiprole – licensed but launch 2015 for CAP/HAP (= linezolid + ceftazidime)
- Ceftazidime – avibactam IV Q1/2’16 – where no other options for cUTI/cIAI – broad activity vs ESBL E.coli & Kleb, PsA and carbapenemases. Some Acin baum activity.
- Eravacycline IV/po 2017 – cIAI by ESBLs = ertapenem

Antimicrobial Stewardship

What is Antimicrobial Stewardship

The term 'antimicrobial stewardship' is defined as 'an organisational or healthcare-system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness'.

NICE AMS Guidelines 2015

Public Health England

NHS

NHS England

Patient Safety Alert

Stage Two: Resources

Addressing antimicrobial resistance through implementation of an antimicrobial stewardship programme

18 August 2015

Alert reference number: NHS/PSA/Re/2015/007

Alert stage: Two - Resources

Antimicrobial resistance (AMR) has risen alarmingly over the last 40 years and inappropriate use of antimicrobials is a key driver[1]. From 2010 to 2013, total antibiotic prescribing in England increased by 6%, comprised of a 4% rise in general practice and a 12% increase in hospital inpatient prescribing[2].

The consequences of AMR include increased treatment failure for common infections and decreased treatment options where antibiotics are vital, such as during certain cancer treatments[3]. Antimicrobial stewardship is key to combating AMR and is an important element of the UK Five Year Antimicrobial Resistance Strategy[4].

Antimicrobial stewardship embodies an organisational and system-wide approach to promoting and monitoring the judicious use of antimicrobials by:

- optimising therapy for individual patients;
- preventing overuse and misuse; and
- minimising the development of resistance at patient and community levels.

This alert has been jointly issued by Health Education England, NHS England and Public Health England (PHE) to highlight the challenge of AMR and to signpost the toolkits developed by PHE to support the NHS in improving antimicrobial stewardship in both primary and secondary care.

Primary care resource (including out-of-hours, urgent care centres and walk-in centres)

- TARGET (Treat Antibiotics Responsibly, Guidance, Education, Tools) (http://www.rcgp.org.uk/clinical-and-research/target-antibiotics-toolkit.aspx) is designed to be used by the whole primary care team within the GP practice or out-of-hours setting, as well as being relevant to mental health care settings. The toolkit aims to help influence prescribers' and patients' attitudes, beliefs and perceived barriers to optimal antibiotic prescribing.

Secondary care resource

- Start Smart then Focus (https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus) provides an outline of evidence-based antimicrobial stewardship practice for use in secondary care settings. The toolkit provides information on strategies to improve antibiotic use within secondary care as well as suggested audits to improve practice.

The actions in this alert will also support the current national work on sepsis to ensure both appropriate antibiotic prescribing and review (https://www.england.nhs.uk/2014/09/02/psa-sepsis/).

These toolkits should be read alongside, "*Clostridium difficile*: how to deal with the problem"[5], "*Clostridium difficile* infection: risk with broad-spectrum antibiotics"[6], and the recently published "Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use"[7].

It is proposed that antimicrobial stewardship management teams/committees, or equivalent, use evidence of implementation of the recommendations in these resources to demonstrate compliance with the Code of Practice on the prevention and control of infections[8].

Actions

Who: All organisations providing NHS funded care where antibiotics are prescribed, dispensed or administered

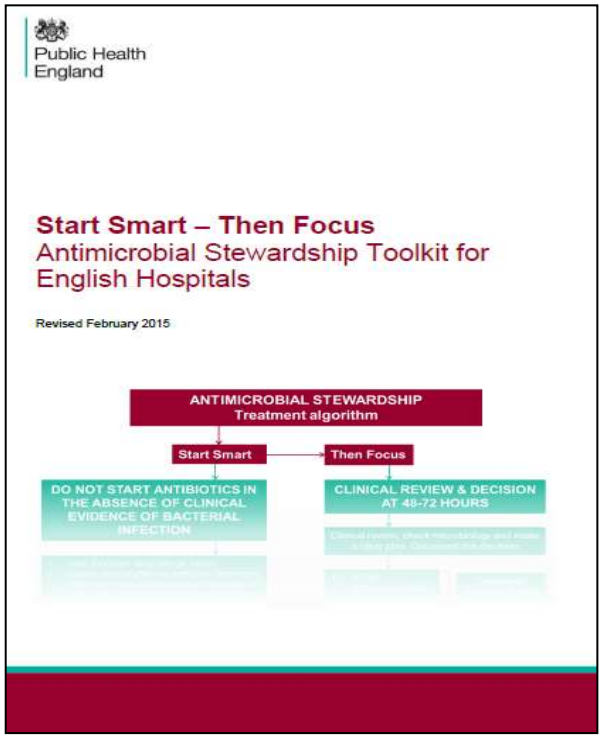
When: To commence immediately and be completed by 31 March 2016

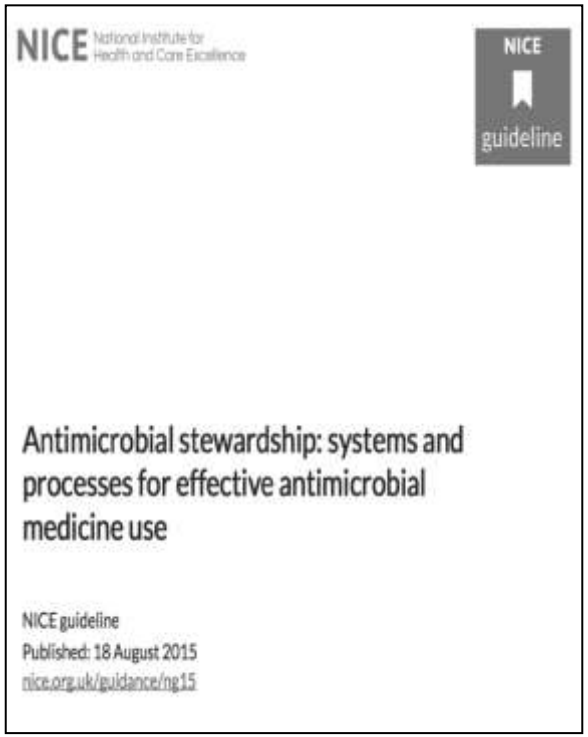
1. Bring this Alert to the attention of those holding leadership roles for antimicrobial stewardship in your organisation (e.g. Directors of Infection Prevention in acute and ambulance trusts, Heads of Medicines Optimisation in acute and mental health trusts, lead GPs and lead pharmacists in primary care).
2. Review the resources signposted in this Alert and through linking with organisational or cross-system antimicrobial stewardship teams/committees, or equivalent, identify how the resources can be used to support your local antimicrobial stewardship programme.
3. By either circulating this Alert or through local alternatives (such as newsletters, local awareness campaigns etc.) ensure that staff are aware of the key antimicrobial stewardship messages and resources relevant to their clinical practice.

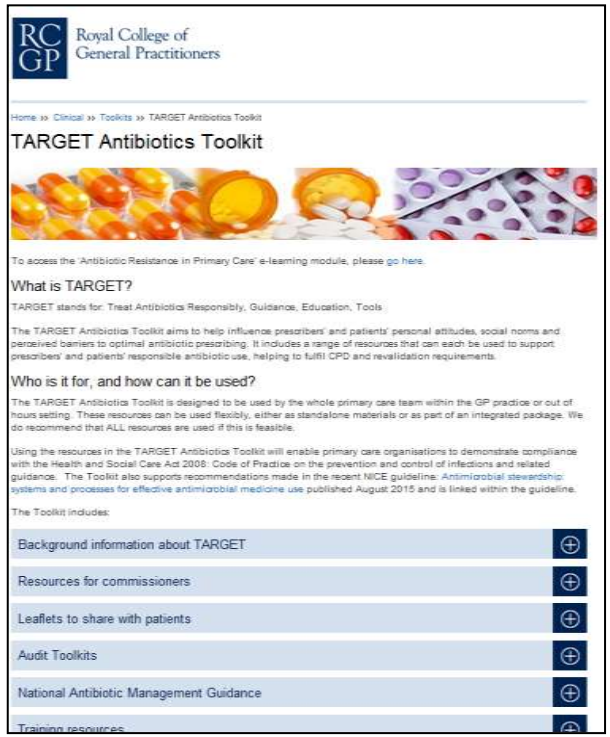
Antimicrobial Stewardship Programme (ASP)

- An ASP describes a bundle of measures that can be adopted to promote the appropriate use of antibiotics, including:
  - evidence-based optimal standards for routine antibiotic use, e.g. correct selection of agent, dose, route of administration and duration of therapy
  - ensuring competency and educational programmes for all staff that use antibiotics
  - communicating antibiotic issues to all stakeholders
  - auditing the impact and uptake of these processes
  - optimising outcomes for patients who receive antibiotics

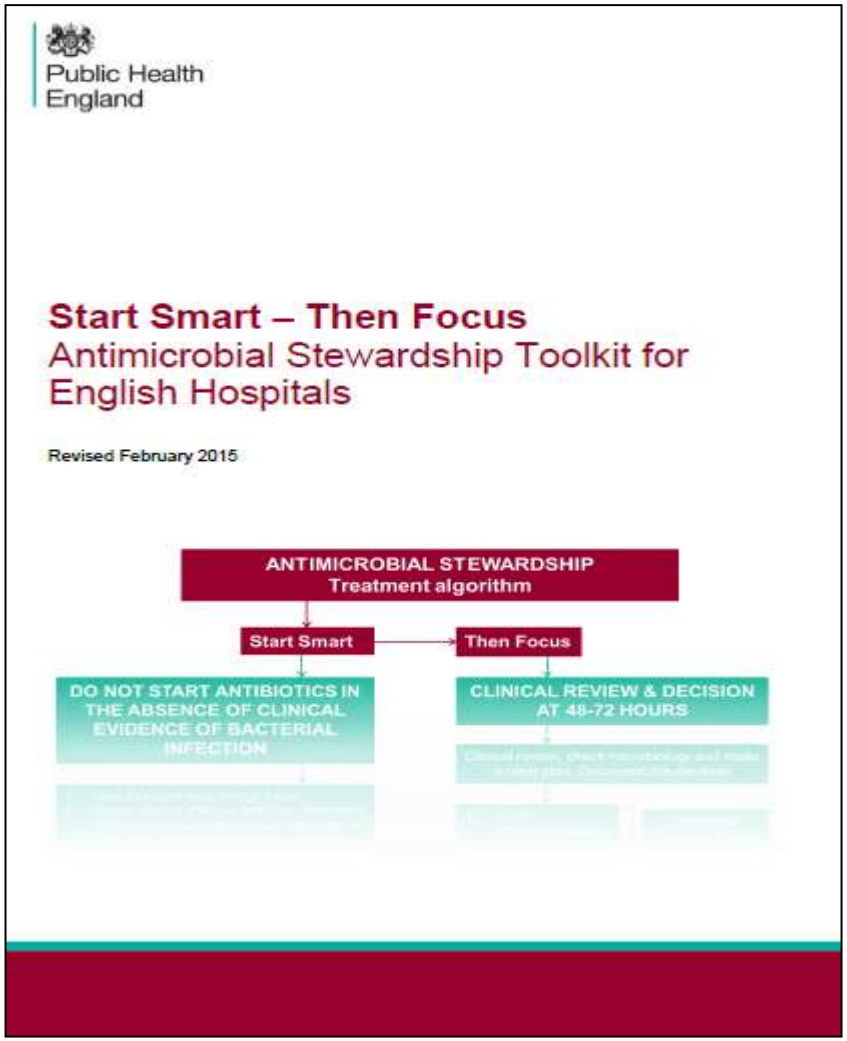
Antimicrobial Stewardship Resources







Antimicrobial Stewardship – Secondary Care Resource



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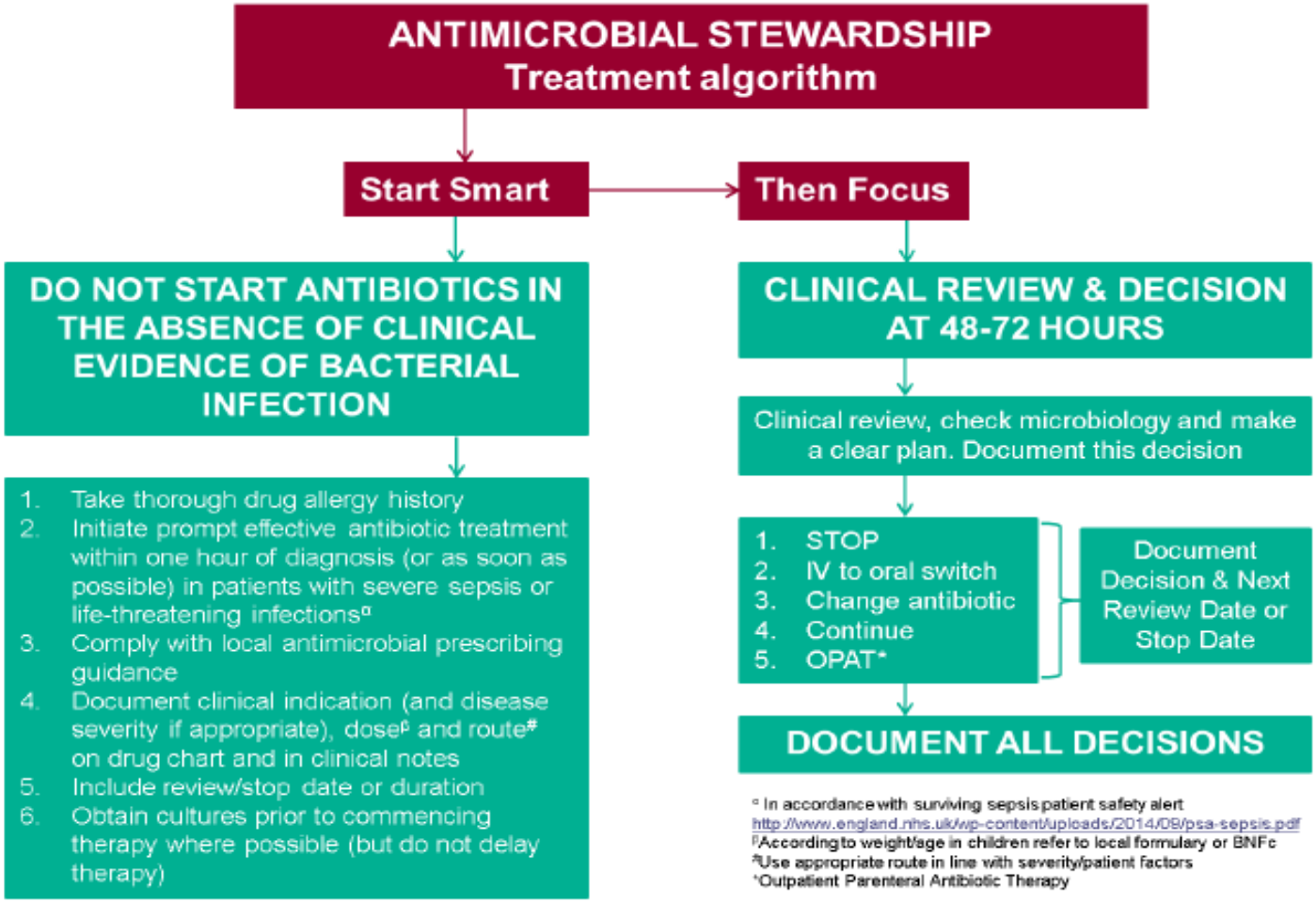
Start Smart Then Focus



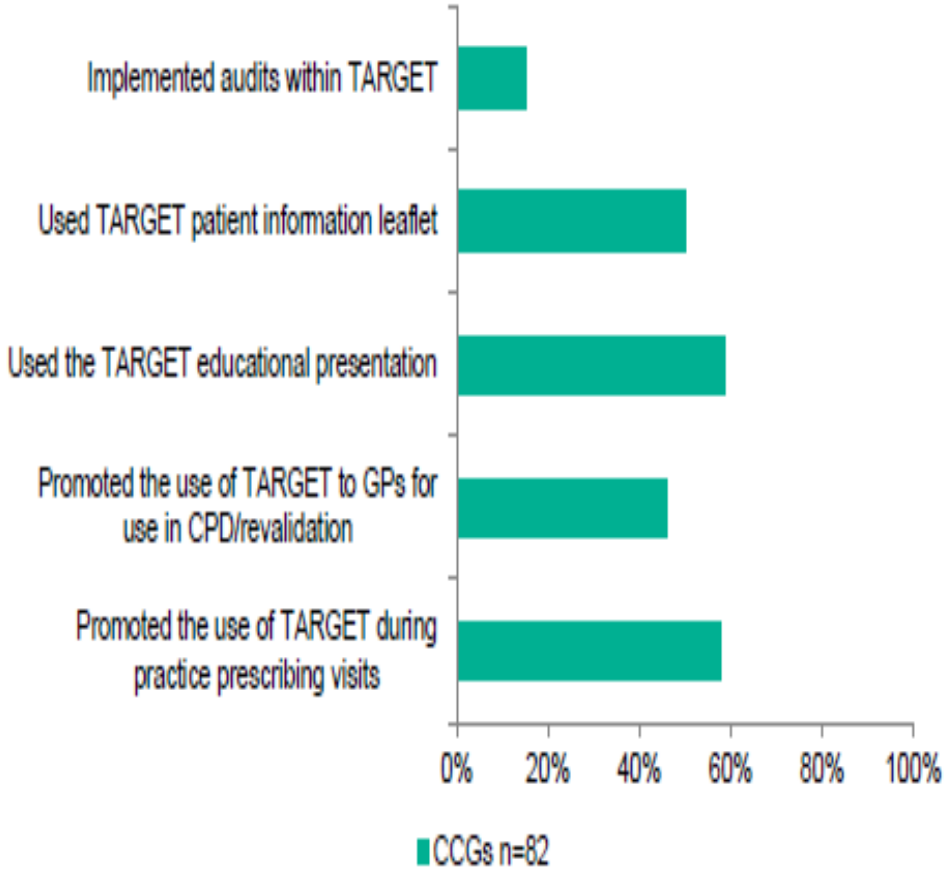


Figure 4.1 Use and promotion of TARGET resources and audits, England, 2014–2015

Antimicrobial Management Team or Equivalent

- Multidisciplinary Group including;
  - Microbiologists/Infectious disease specialist
  - Antimicrobial pharmacist
- Evidence based local antimicrobial guidelines
- Audit
- Antibiotic consumption data
- Targeting high risk antibiotics
- Ward based activities
- Education and Training
- Incentive schemes
- Pathway review – really important to develop this
- Use of TARGET/SSTF resources
- Promoting vaccination
- Lots of collaboration - development of AMS networks

NHSE Antibiotic Quality Premium 2015-16
and what it means for CCGs

The Quality Premium is intended to

- Improve the quality of services commissioned, improving health outcomes and reducing inequalities in health outcomes
- Reward CCGs for quality improvement, paid in the following financial year, and must be reinvested in quality or health outcome improvement
- Reduction in the number of antibiotic prescriptions by 1% as measured by the NHS BSA antibacterials per STAR-PU
- Reduction in the proportion of broad spectrum antibiotics cephalosporins, quinolones & co-amoxiclav by 10% or to below England median value = 11.3%
- FY 2015-16

NHS England

National Antibiotic Quality Premium Dashboard

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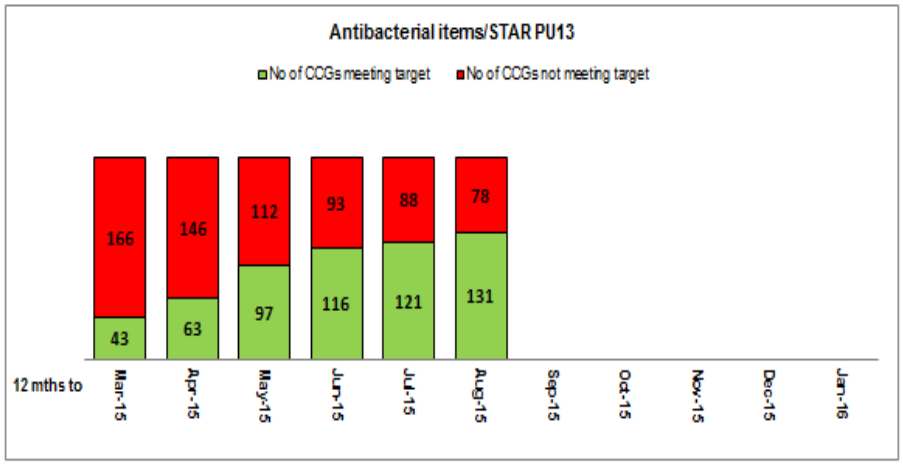
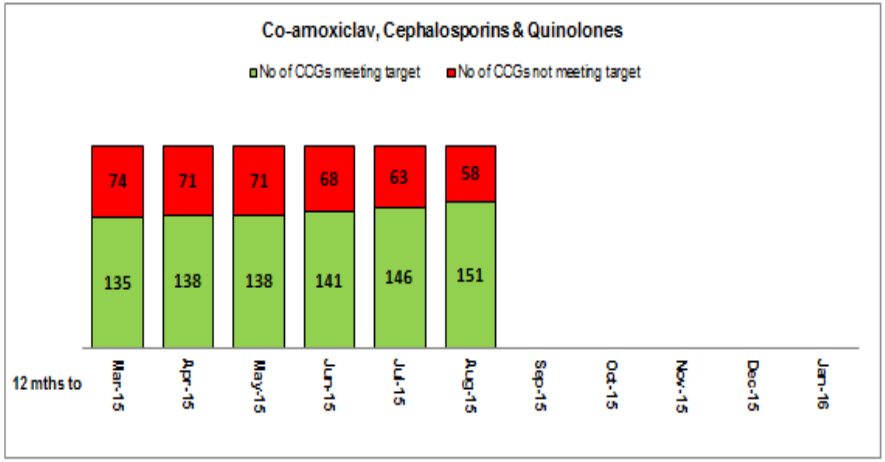
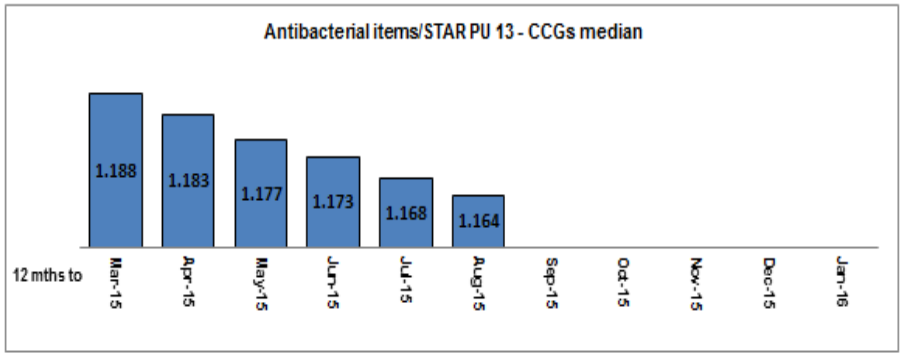
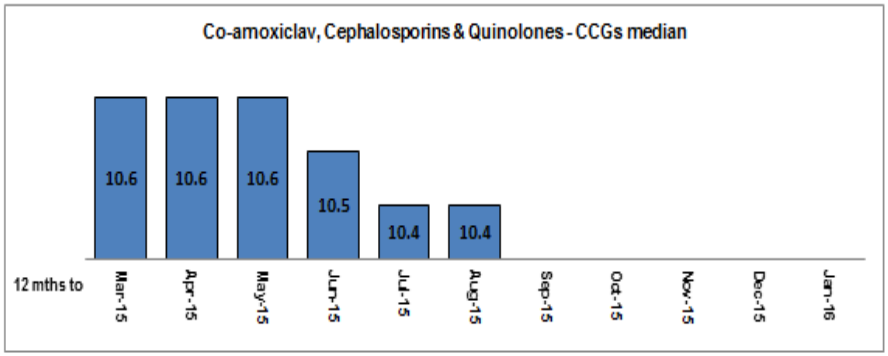
NHS England

NHS Business Services Authority









https://www.england.nhs.uk/resources/resources-for-ccgs/ccg-out-tool/ccg-ois/anti-dash/

Education and Training

- Teaching programme
  - Doctors
  - Nurses
  - Pharmacists
  - Other Health Care Professionals
- European Antibiotic Awareness Day (EAAD)
- Antibiotic Guardian
- E-learning

Antimicrobial Prescribing and Stewardship Competencies

1. Infection prevention and control
2. Antimicrobial resistance and antimicrobials
3. Prescribing antimicrobials
4. Antimicrobial stewardship
5. Monitoring and learning

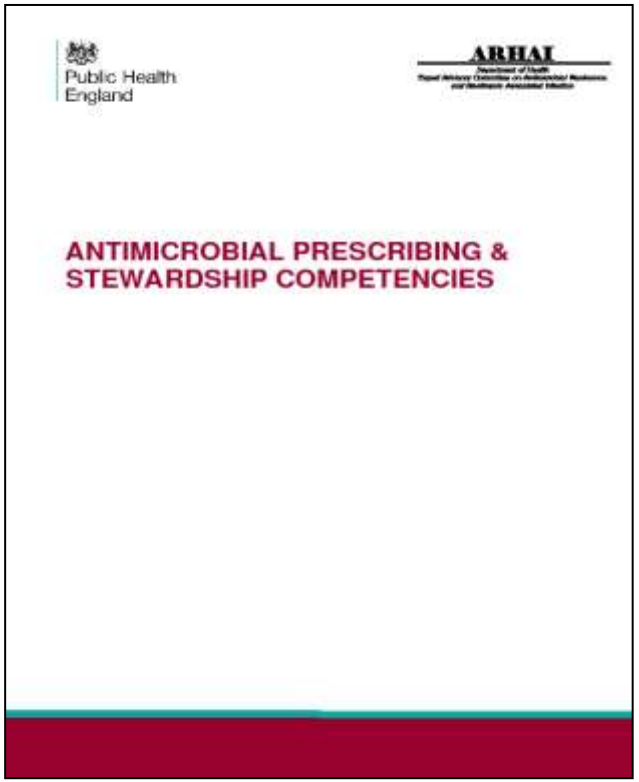


Table 0.3 Comparison of antimicrobial stewardship activities in secondary and primary care, England, 2014

	Secondary care: Acute NHS Trust n=100	Primary care: Clinical commissioning groups n=82
Existence of AMS committee	94%	18%
Written dedicated antimicrobial policy	93%	99%
Action plan/Implemented toolkit	46%	13%
Written education and training strategy	24%	1%
Implemented audits within AMS toolkit	74%	15%

Become an Antibiotic Guardian Champion

ANTIBIOTIC GUARDIAN
UK SUPPORT FOR EUROPEAN ANTIBIOTIC AWARENESS DAY

- **European Antibiotic Awareness Day** (EAAD) takes place annually on **18 November**
- **As an Antibiotic Guardian**, choose a simple action based pledge and encourage others to join you in protecting antibiotics against the growing threat of antibiotic resistance at: **www.antibioticguardian.com**
- **Resources and promotional materials** to support local activities for Antibiotic Guardian and EAAD are available via **www.antibioticguardian.com**
- The Antibiotic Guardian campaign was established by PHE to improve public and professional knowledge and stimulate engagement on tackling antibiotic resistance
- Public Health England is leading the co-ordination of EAAD activities in England in collaboration with VMD, Department of Health, devolved administrations, and other professional organisations

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