Medicine

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Antimicrobial resistance UK national policy

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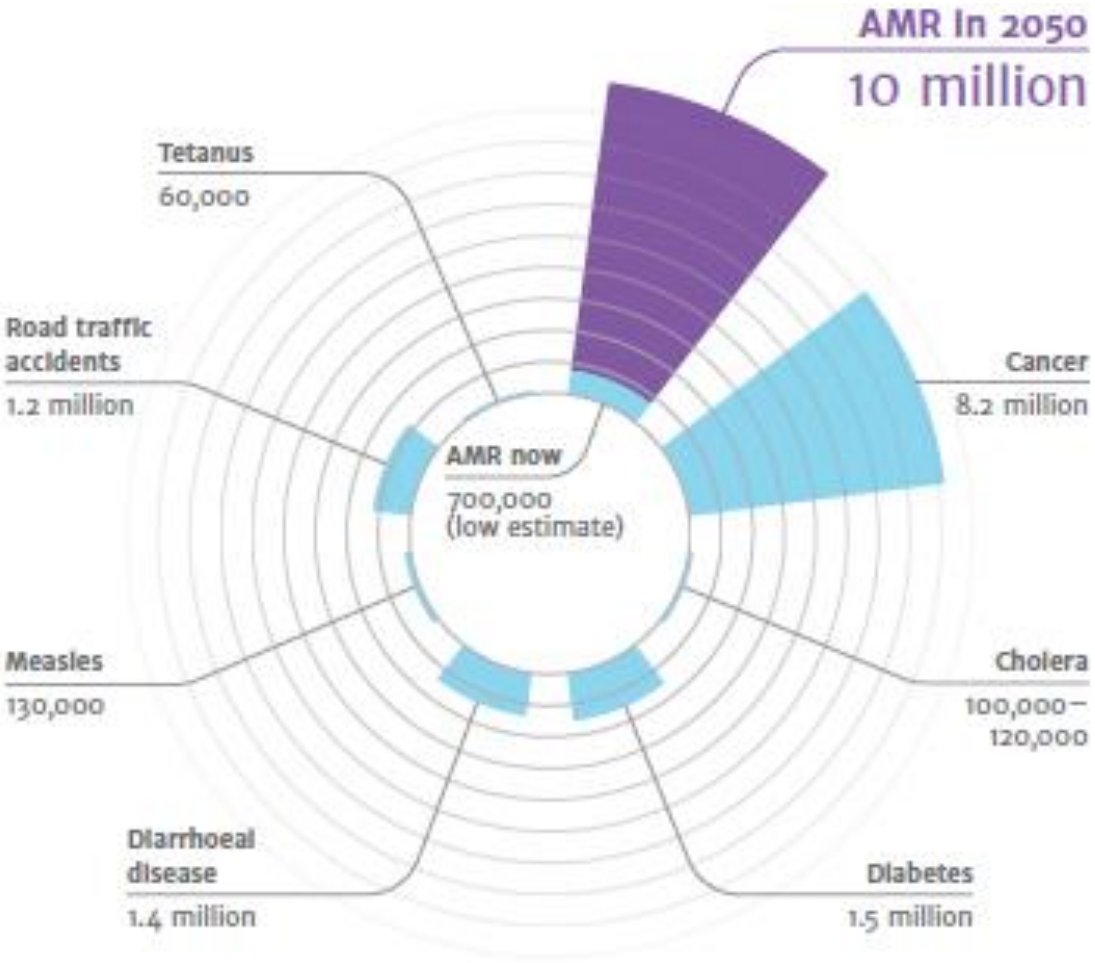
UKCRC Registered Clinical Trials Units

NHS National Institute for Health Research

Deaths attributable to Antimicrobal resistance every year



What was the world like before antibiotics?

- Before introduction of antibiotics (1940s), it was “normal” for patients in the UK to die from sepsis, endocarditis, etc.

The Willcox family, 1916

Antibiotics should be for saving lives…

Professor Sir Howard Florey, BMJ, 1944:

Bacteria Sensitive to Penicillin

Gram-positive.—*Streptococcus pyogenes, Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus viridans, Bacillus anthracis, Corynebacterium diphtheriae, Actinomyces bovis, Clostridium tetani, Cl. welchii, Cl. septique, Cl. oedematiens.*

Gram-negative.—*Neisseria gonorrhoeae, N. meningitidis.*

STREPTOMYCIN IN SUBACUTE BACTERIAL ENDOCARDITIS

REPORT OF THREE CASES

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PENICILLIN treatment has proved so successful in subacute bacterial endocarditis that a high probability of cure may be entertained in cases diagnosed early; but success, which can in no case be guaranteed, depends on early treatment, on sufficiently large and prolonged dosage, and on the penicillin sensitivity of the organism (Christie 1948, 1949).

Some cases not only fail to respond but become worse in spite of such treatment, and may yet be saved by the use of streptomycin. The following three cases

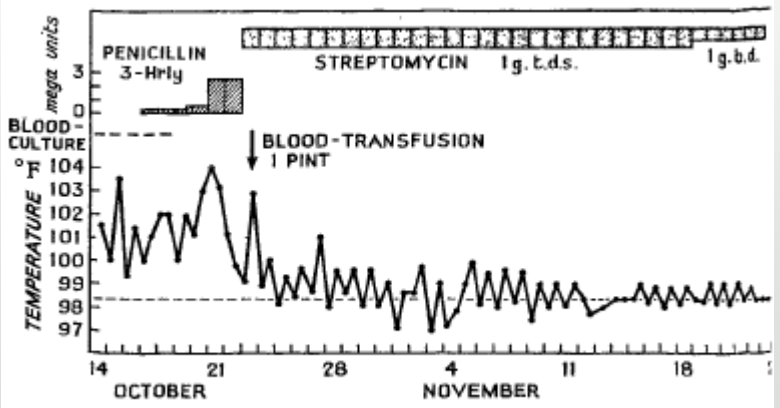
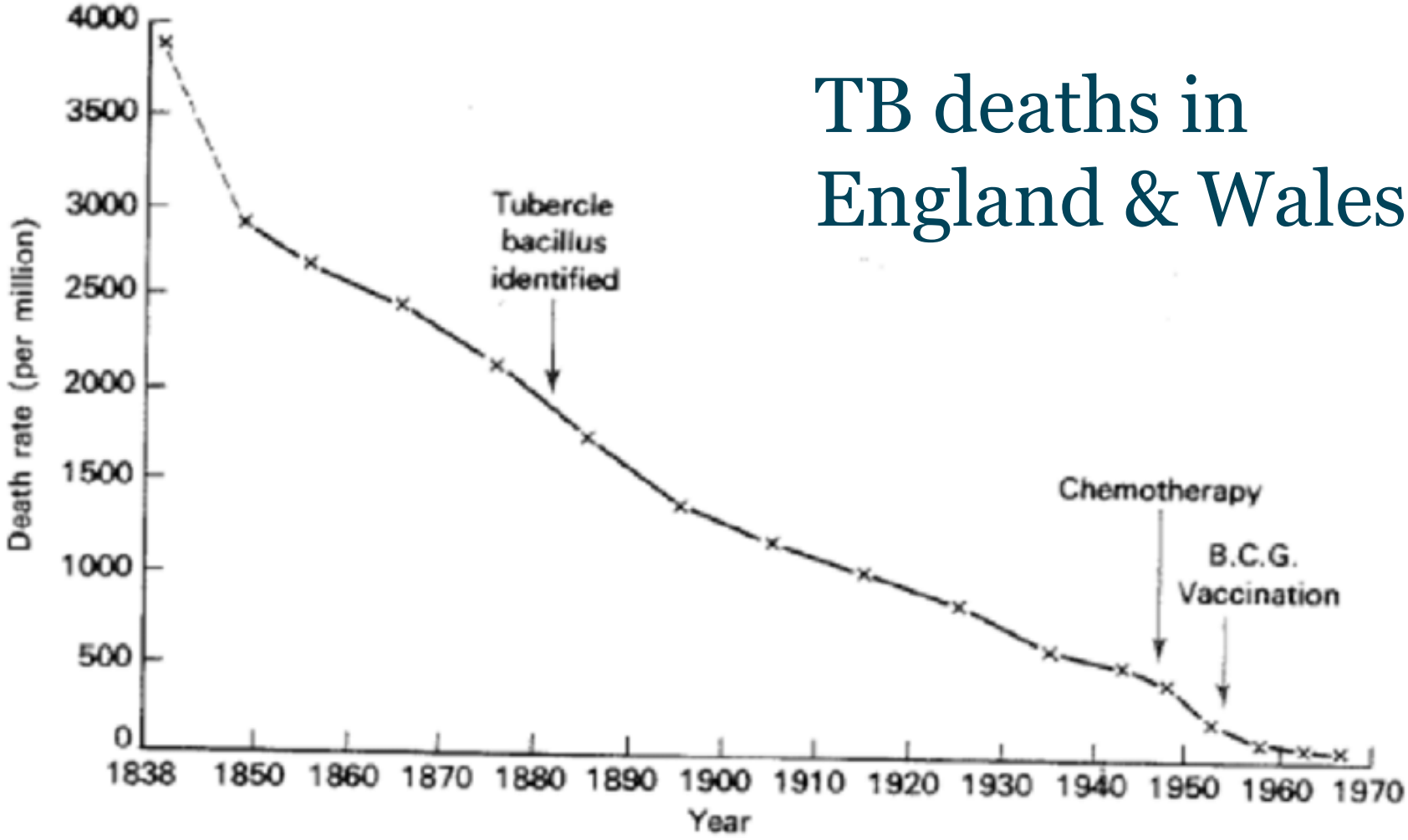


Fig. 2—Temperature and treatment chart of case 2.

TB deaths in England & Wales



5.1 Respiratory tuberculosis: death rates, England and Wales.

Clinical case - 2019

- 7 year old girl presents with urinary symptoms (dysuria, increased frequency)
- Treated empirically with trimethoprim, urine sample sent to lab
- 2 days later calls back because is not improving
- Urine results: E. coli, resistant to amoxicillin, trimethoprim, nitrofurantoin.
- Treated with co-amoxiclav

Deaths attributable to Antimicrobal resistance every year

123 countries report extensive multi-drug resistant TB (MDR-TB)

up to 2bn people, mainly in LMICs, lack access to antimicrobials

0 new class of antibiotics discovered and available for routine treatment since the 1980s

700k people are estimated to die each year from drug-resistant infections

3x rise in global antibiotic consumption is predicted by 2030

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Impact of AMR on Sustainable Development Goals

- AMR strikes hardest on the poor; treatment of resistant infections is more expensive

- Untreatable infections in animals threatens sustainable food production for growing populations

- Antimicrobials are fundamental components of all health systems

- Clean water and effective sanitation reduces infections and antibiotic residues from multiple sources contaminate water

- Cost of AMR is predicted to be US$100 trillion by 2050, driving an extra 28 million people into poverty

- It is crucial to balance access and conservation of antimicrobials with innovation, to contain AMR

Source: based on World Health Organisation

Previous national action plans

- UK has had NAP on AMR since 2000

THE UK'S 2013–2018 AMR STRATEGY: A RE-CAP

The UK's 2013-2018 AMR strategy included three strategic aims, underpinned by actions in seven key areas.

Aims:

- Improve knowledge and understanding of AMR.
- Conserve and steward effectiveness of treatments.
- Stimulate development of new products.

Action areas:

1. Improve infection prevention and control practices.
2. Optimise prescribing practice.
3. Improve professional education and public engagement.
4. Develop new drugs, treatments and diagnostics.
5. Better access and use surveillance data.
6. Better identify and prioritise AMR research needs.
7. Strengthen international collaboration.

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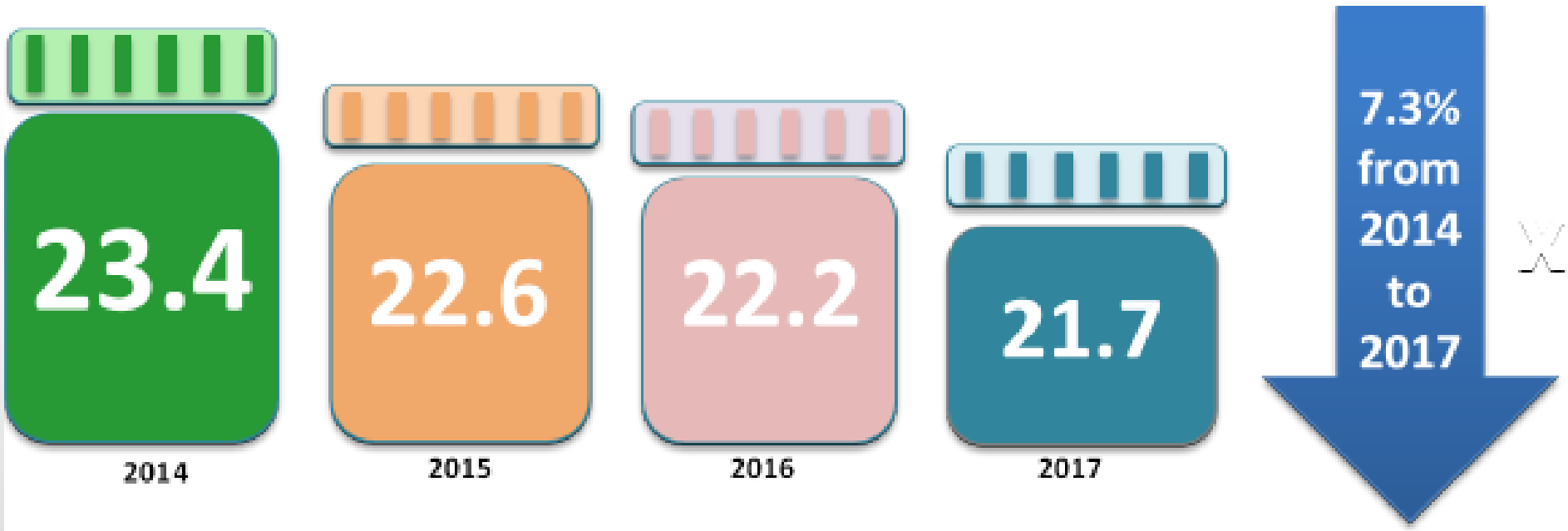
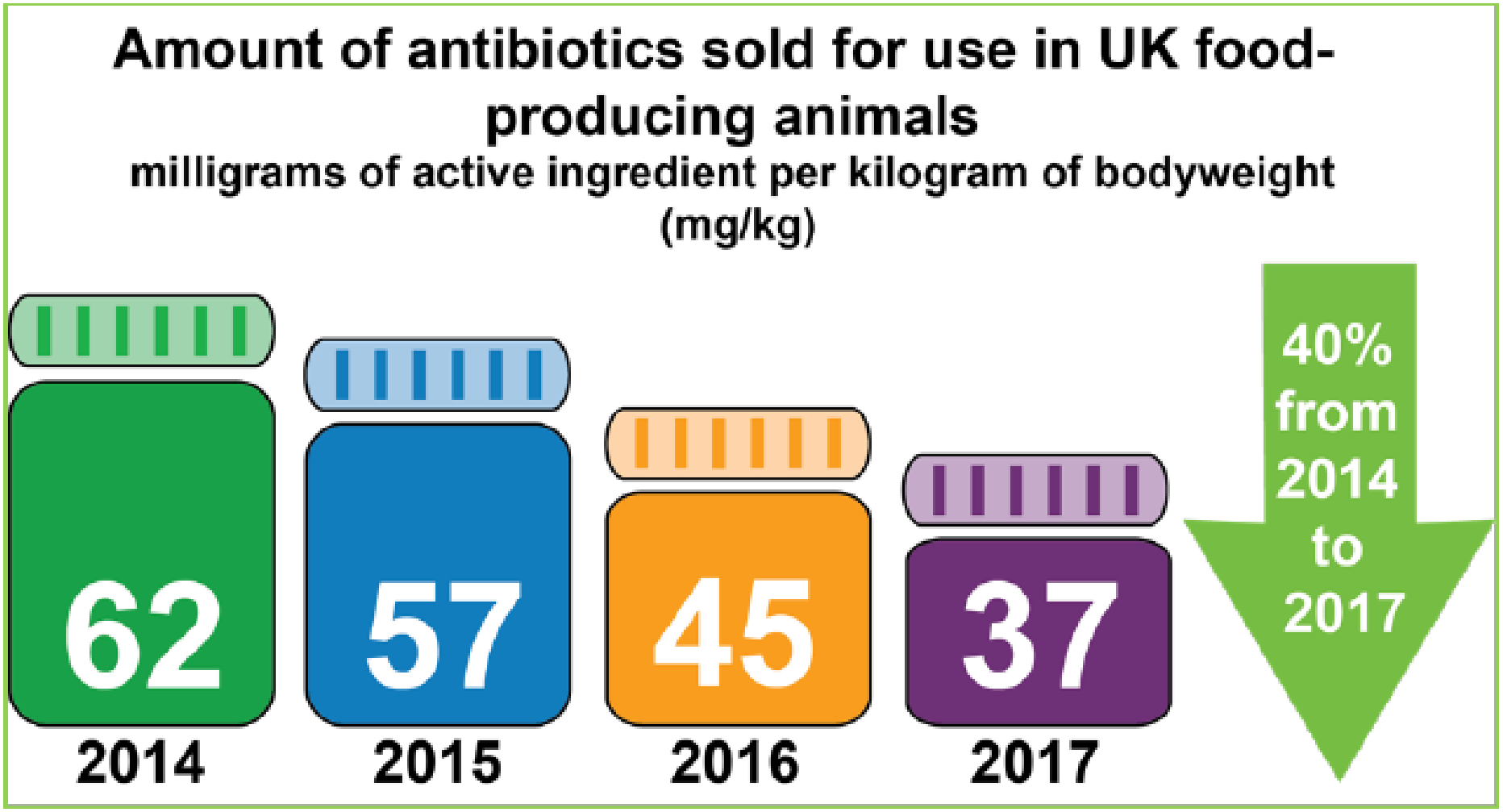
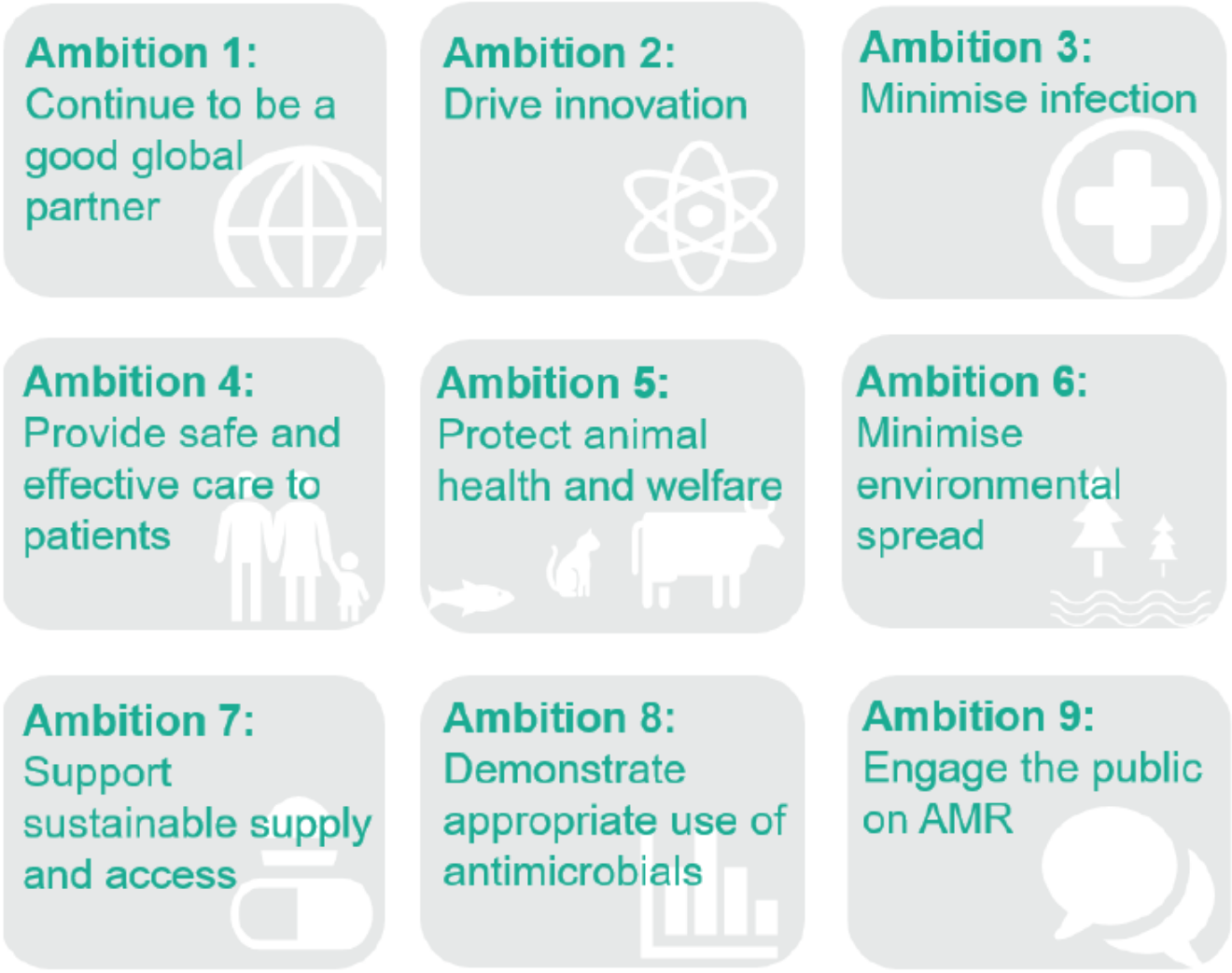
Amount of Antibiotics consumed in the UK

Defined Daily Doses per 1000 inhabitants per day




Amount of antibiotics sold for use in UK food-producing animals
milligrams of active ingredient per kilogram of bodyweight (mg/kg)
62
57
45
37
2014
2015
2016
2017
40% from 2014 to 2017

UK's 20-year vision for AMR



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HM Government

Tackling antimicrobial resistance 2019–2024

The UK's five-year national action plan

Published 24 January 2019

Content areas

What needs to be done to tackle AMR

1. Reduce need and unintentional exposure

- Lower burden of human infection
- Clean water and sanitation
- Lower burden of animal infection
- Minimal environmental impact
- Better food safety

2. Optimise use of antimicrobials

- Optimal use in humans
- Optimal use in animals & agriculture
- Lab capacity & surveillance in humans
- Lab capacity & surveillance in animals

3. Invest in innovation, supply and access

- Basic research
- Development of new therapeutics
- Wider access to therapeutics
- Development of & access to diagnostics
- Development of & access to vaccines
- Better quality assurance

Levers

Ways of addressing content areas

1. Awareness & capacity building
2. Measurement & surveillance
3. Funding & financial incentives
4. Policy & regulation
5. Championing & piloting

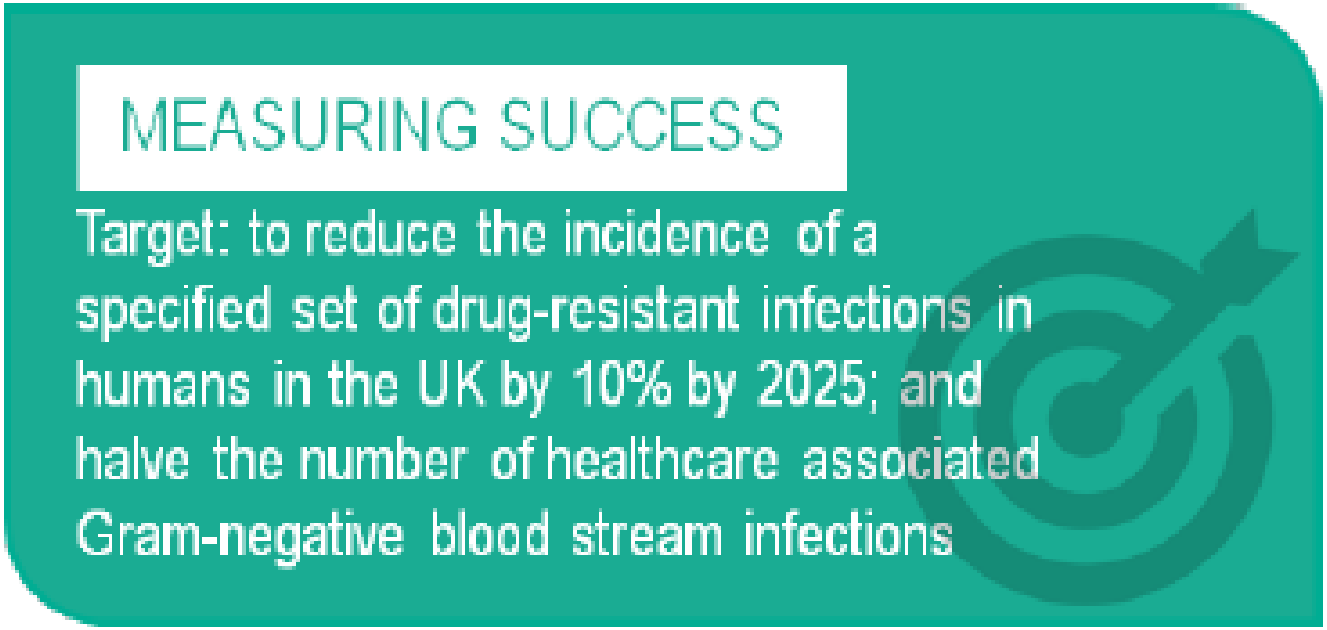
Enablers

Preconditions needed to apply levers successfully

1. NAPs, systems strengthening & SDG alignment
2. Global governance & coordination
3. Coalition building & political commitment

Reducing need for, and unintentional exposure to, antimicrobials

- Lower burden of human infection
  - Strengthen Infection prevention and control for priority infections (eg Gram negative sepsis)



Reducing need for, and unintentional exposure to, antimicrobials

- Lower burden of human infection
  - Improve professional capacity for infection prevention and control (IPC)
    - Training in handwashing
    - Regulatory inspections and audits (CQC)
  - Improving IPC practice in the public
    - Teaching about hand hygiene in schools
  - Turn research into practice for IPC – behaviour change

Reducing need for, and unintentional exposure to, antimicrobials

UK Aid for WASH

- UK Aid supports community WASH programmes in **more than 20 countries**
- This will help more than **60 million people** gain access to basic WASH facilities by 2020.
- UK Aid also runs two centrally-run programmes that work across **13 countries** to deliver sustained access to WASH.
- In 2015, UK Aid provided **£183 million** of water/WASH-related bilateral and multilateral financial assistance.

Reducing need for, and unintentional exposure to, antimicrobials

- Lower burden of human infection
- Greater global access to clean water and sanitation
- Lower burden of animal infection

Reducing exposure

- Good hygiene
- Animal housing design & build
- Group management
- Minimum movement & mixing
- Biosecurity

Reducing susceptibility

Reducing need for, and unintentional exposure to, antimicrobials

- Lower burden of human infection
- Greater global access to clean water and sanitation
- Lower burden of animal infection
- Minimise spread of AMR through the environment
  - Monitoring antibiotics in the water supply
  - Sourcing antibiotics from responsible companies

Reducing need for, and unintentional exposure to, antimicrobials

- Lower burden of human infection
- Greater global access to clean water and sanitation
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- Minimise spread of AMR through the environment
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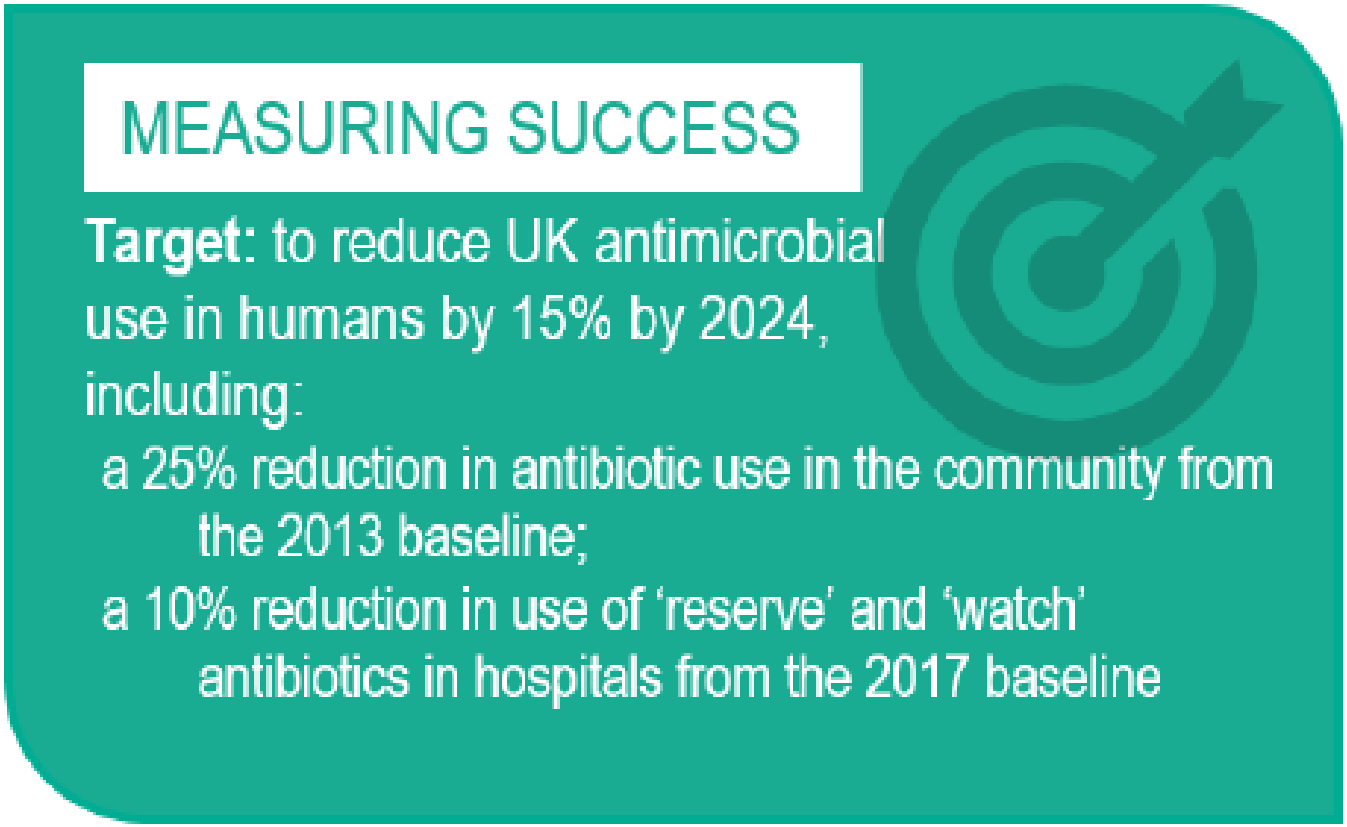
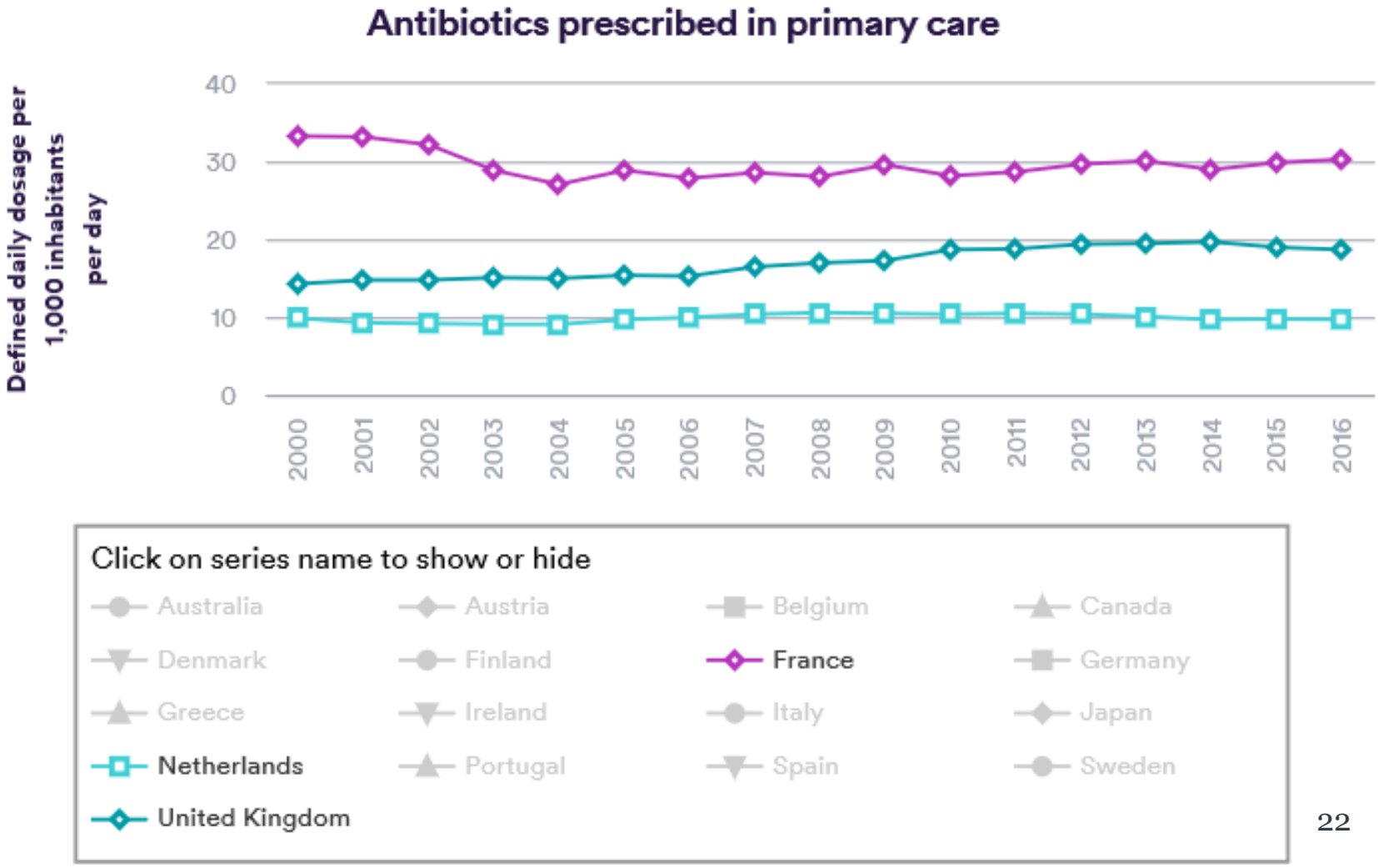
Optimising use of antimicrobials

- Optimal use of antimicrobials in
  - humans

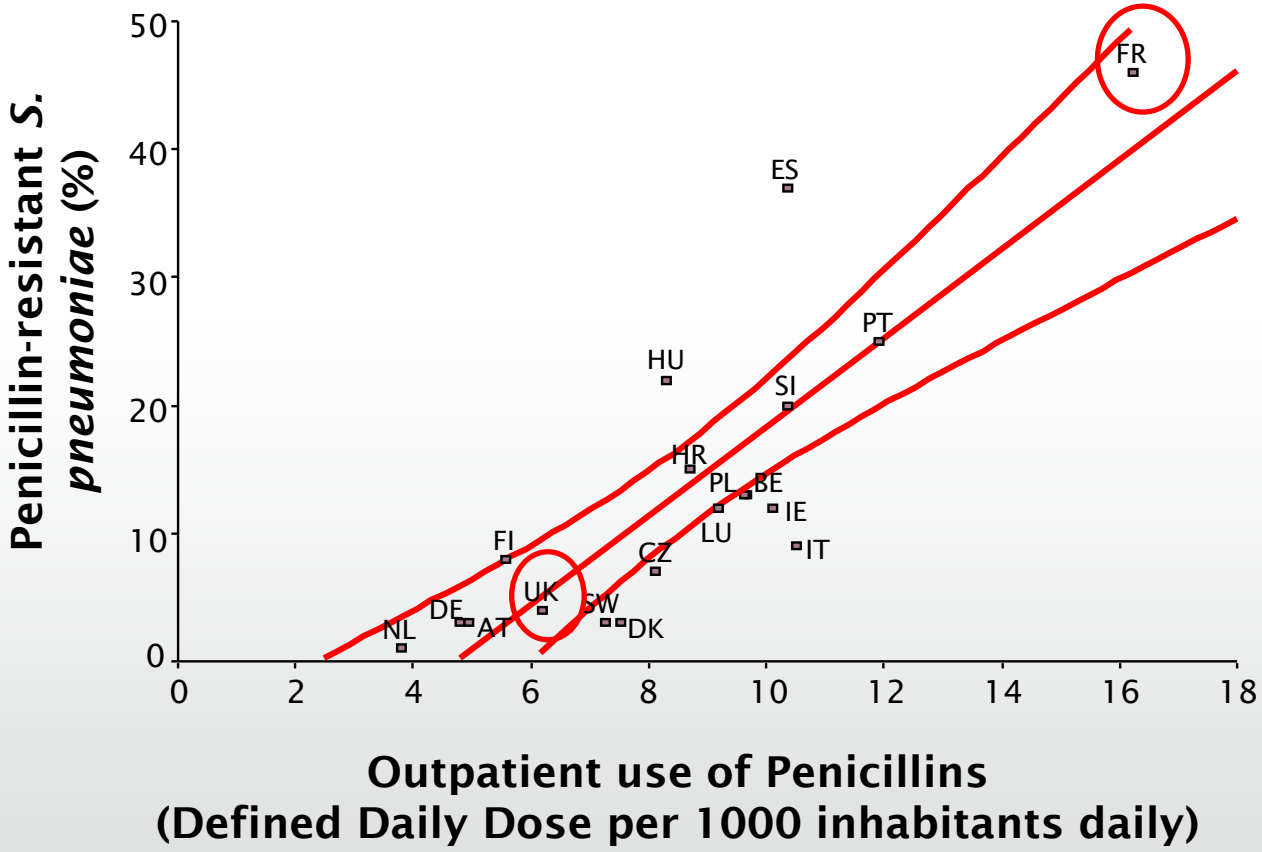


Antibiotic use in different European countries



High use = High resistance

Penicillin Use correlates with prevalence of penicillin-resistant *Streptococcus pneumoniae*



Goossens H, et al. *Lancet.* 2005; 51: 365(9459):579-587.

What are we using antibiotics for?

- In England, 74% of human antibiotics are prescribed in general practice (ESPAUR report, 2016)
- The majority are prescribed for minor self limiting conditions
- 20% of antibiotics prescribed in UK primary care are unnecessary

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Antibiotic stewardship: The AWaRe index

First and second choice antibiotics for treating the most common infections.

Includes: amoxicillin for pneumonia and penicillin for streptococcal sore throat

Antibiotics with higher resistance potential, that should only be prescribed for specific indications.

Includes: ciprofloxacin in the treatment of complicated UTI

Antibiotics that are last-resort options that should only be used in severe circumstances, when other options have failed.

Includes: colistin and IV parental fosfomycin

Promoting evidence-based guidance

CASE STUDY **NHS England QP (Quality Premium) and CQUIN (Commissioning for Quality and Innovation)**

Quality Premium in primary care from 2015
Year 1: 96% CCGs met or exceeded the target of a 1% reduction in prescribing from a 2013/14 baseline delivering an 8.3% reduction nationally, or the equivalent of 2.7 million antibiotic items.

Year 2: 88% CGGs met or exceeded a 'stretch' reduction target of 4% from baseline.

After 2 years, prescribing of '**broad spectrum**' antibiotics had **reduced by 23%;** a reduction of 904,881 items.

Total payments made to CCGs: £15.9m; total prescription and dispensing costs avoided estimated at £19.3m.

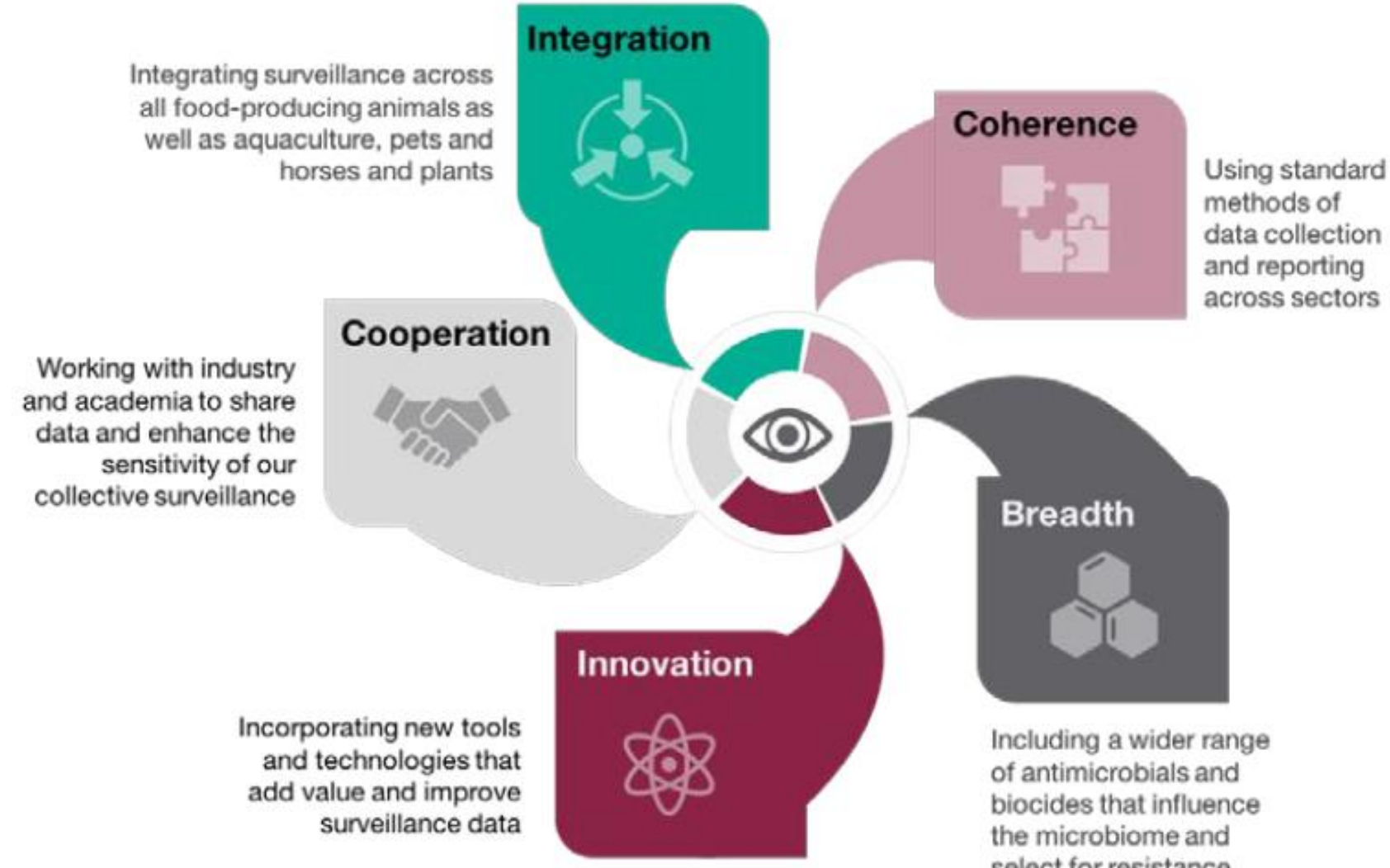
Optimising use of antimicrobials

- Optimal use of antimicrobials in
  - humans
  - animals and agriculture
  - Target: **Reduce UK antibiotic use in food-producing animals by 25% between 2016 and 2020** and define new objectives by 2021 for 2025

How to reduce use of antibiotics in animals?

- Use for growth promotion is now banned in the UK
- Increasing use of vaccines
- Targeted treatment to eradicate disease
  - E.g. eradication of enzoonotic pneumonia from 6 large pig herds (5000 sows)
  - Avoids need to treat the 125 000 piglets produced each year
  - Average antibiotic use reduced from 120mg/kg to 30mg/kg

Optimising use of antimicrobials



Investing in innovation, supply and access

- Sustainable investment in basic research
- Development of new therapeutics

PROJECTS

276 projects target infectious disease

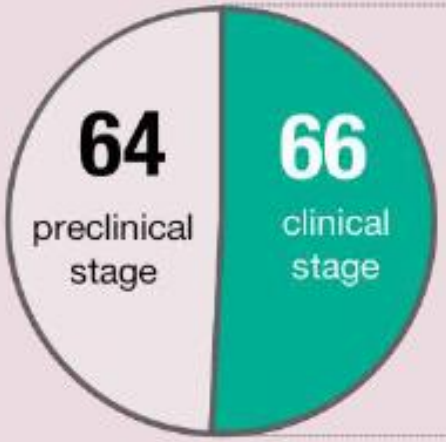
130 target priority bacteria

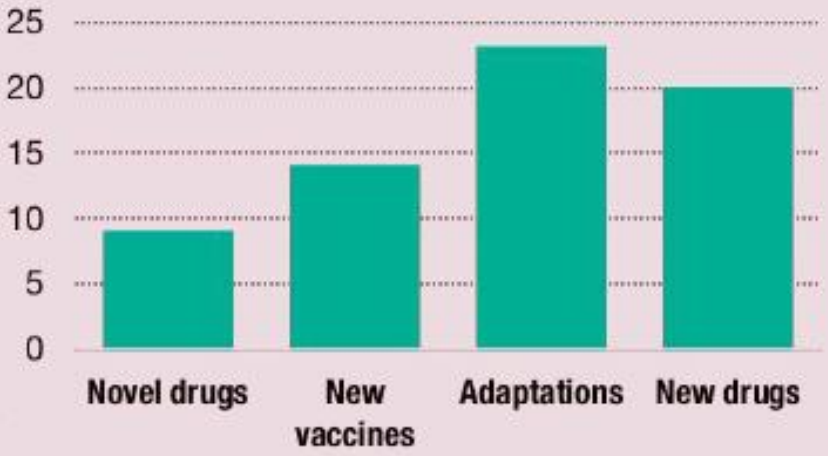
30 companies in scope

147 projects target bacteria

54 target gram-negative bacteria

PRIORITY BACTERIA FOCUS





Investing in innovation, supply and access

- Sustainable investment in basic research
- Development of new therapeutics
- Wider access to therapeutics for those who need them
- Development of, and access to, diagnostics
  - Target: Be able to report on % of prescriptions supported by a diagnostic test or decision support tool by 2024

Sore throat: test or decision support tool?

Clinical score and rapid antigen detection test to guide antibiotic use for sore throats: randomised controlled trial of PRISM (primary care streptococcal management)

- Targeted use of antibiotics for acute sore throat with a clinical score (FeverPAIN) improves reported symptoms and reduces antibiotic use.
- Antigen tests have no clear advantages over a clinical score alone.
- Little et al, BMJ 2013.

Launched in 2014

£10m Prize fund for novel diagnostics to tackle AMR

77 Teams registered to compete across 14 countries

29 Seed grants allocated

£8m Prize fund

Criteria

- Novel
- rapid (within 30 minutes),
- Affordable,
- Accurate
- Safe

- Connected
- Easy to use
- Scalable
- Available globally

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- Development of, and access to, vaccines
- Better quality assurance of AMR Health products

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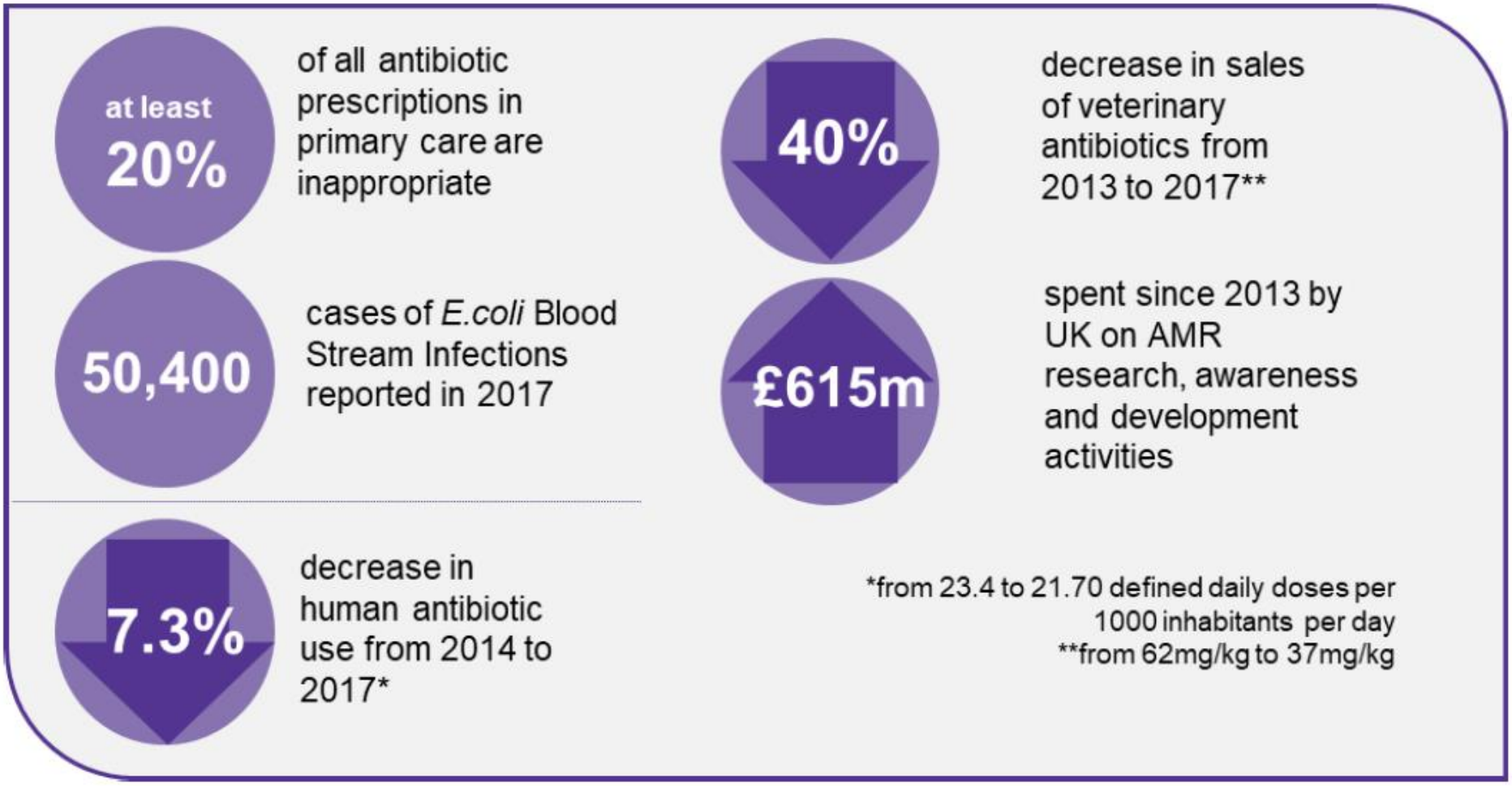
Summary: AMR in the UK



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