The use of diagnostics in addressing antimicrobial resistance

Fiona Carragher FRCPath   @DepCSOFiona
Deputy Chief Scientific Officer for England

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The ‘neck and neck’ race of antibiotic development - and resistance

Introduction of new antibiotic classes

1935 sulfonamides
  1941 β-lactams
  1944 aminoglycosides
  1947 nitrofurans
  1949 chloramphenicol

1950 tetracyclines
  1952 lincosamides
  1952 streptogramins

1956 glycopeptides
  1957 ansamycins
  1959 nitrimidazoles

1962 quinolones
  1963 trimethoprim

1970s

1980s

1990s

2000s

2003 lipopeptides
  2000 oxazolidinones

Development of bacterial resistance

1940 Penicillinase
  1942 sulfonamide resistance
  1947 streptomycin resistance

1953 macrolide resistance

1961 methicillin resistance
  1966 nalidixic acid resistance
  1968 tetracycline resistance
  1969 aminoglycoside modifying enzymes

1981 Amp C β-lactamase
  1983 ESBL
  1988 VRE

1990s fluoroquinolone resistance
  1997 VISA

2000s resistance against linezolid and daptomycin
  2002 VRSA
The challenge of 21st Century antibiotic use

- 35,000 or 7% of all deaths in the UK are caused by infectious diseases.
- 66 different antibiotics prescribed - top 15 account for 98% in general practice and 88% in hospitals.
- 35 million courses of antibiotics are prescribed by GPs in England each year.
- Without antimicrobials, the rate of post-operative infection for clean surgery could be 0-50%. ~30% of those with a serious infection would die.
The rising tide of Antimicrobial resistance

- Infections are increasingly developing that we cannot treat with a rapid spread of multi-drug resistant (MDR) bacteria
- We may not be able to treat of prevent everyday infections or disease
  - Existing antimicrobials are becoming less effective
  - Bacteria, fungi, viruses are adapting naturally and becoming increasingly resistant
  - Inappropriate use of these medicines
  - All-time low in new antibiotics being developed

Recognising this is a ‘one health’ agenda

Who priority list of 12 resistant bacteria that pose the greatest threat to human health
www.who.int
The future if we do not act now

By 2050: more deaths from resistant infections than cancer
UK response to this challenge

- Improving infection protection and control
- 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
- Strengthened international collaboration

Progress against the strategy is reported on an annual basis
Leading worldwide action on antimicrobial resistance

- UK Chief Medical Officer Dame Sally Davies has led a worldwide campaign to take action on antimicrobial resistance
- **Sep 2016**: 193 countries signed a United Nations declaration at the UN General Assembly in New York
- For the first time, Heads of State committed to taking a broad, coordinated approach to address the root causes of AMR across multiple sectors, especially human health, animal health and agriculture.
Independent review of Antimicrobial Resistance - Jim O’Neill

• Diagnostics are critical to the appropriate use of antimicrobials
• Step change in the way technology is incorporated into the decision making process
• Currently many decisions are based on an empirical diagnosis
• Rapid point of care diagnostics enabling a precise, timely diagnosis
• Decision support approach to drive change in prescribing

“I call on Governments to ensure that, by 2020, all antibiotic prescriptions will need to be informed by …. a rapid diagnostic test wherever one exists”  Jim O’Neill

“Having rapid, low-cost, and readily available diagnostics is an essential part of the solution to this urgent problem.”  Dr Margaret Chan, DG, World Health Organisation
Role for diagnostics

- Avoiding unnecessary treatment
- Optimising patient treatment & use
- Identifying high-risk patients
- Improving drug development & stewardship
- Screening
Overview of activity

National ambitions
1. Halve gram –ve HCAI blood infections by 50% by 2020
2. Halve inappropriate prescribing in humans by 2020
3. Reduce animal antibiotic use to 50mg/kg by 2018
4. Work internationally to bring new products to market
UK AMR Diagnostics Vision

“This strategy will tackle the issues around AMR through patient-centred, cost effective diagnostics by ensuring that the right test is available at the right place at the right time.

“It will maximise the use of available technologies in human & animal health sectors in the most appropriate settings.”

The vision will be delivered through a coordinated & consistent national approach to standards & practice

- In every part of the country, in every healthcare setting, the same level of access to rapid diagnostic technology & digital antimicrobial guidance tools are available
- The technology meets nationally set standards of quality & response times
- There is recognition that different settings might need different technical solutions
- Services are flexible & responsive to the adoption of new technologies that will provide continuous improvement
UK AMR Diagnostics strategy

Ensuring that the **right test** is available at the **right place** at the **right time**.

- Self-care & monitoring
- Pharmacy & other high street services
- Primary and Community Care
  - We need to capture good practice examples
  - Linked to changing behaviours and targeted education and training
- Secondary and Tertiary Care
- Public health & surveillance
  - Linked through integrated data-sharing
  - Coordinated by coherent commissioning
Which markers should we measure?

- **Susceptibility** (*which antibiotics can I use?*)
- **Resistance** (*which antibiotics must I not use?*)
- **Bacterial type**
- **Bacterial or viral**

From O’Neill [http://amr-review.org/]
Key areas for action

Understanding the clinical pathway
Where are the diagnostics gaps?
Innovation Evaluation Adoption
Professional and public behaviour
Commissioning and investment

Public Health Intelligence
One Health agenda
Putting diagnostics at the centre of AMR management

A map of the Sepsis pathway across home and hospital
Integration & collaboration is needed to deliver across the innovation pipeline.
Opportunities through new diagnostics

Handheld ‘lab on a chip’
- Coupling smartphones with ‘lab on a chip’ technology for tests
- Egg gene arrays
- Still at research stage but show great potential

Point of care testing
- Well established for indirect technologies such as CRP testing.
- Developments in microarrays offer increased potential for direct testing

High throughput genomic technologies
- Delivers rich direct testing, allowing detailed identification & surveillance
- Seeing advances in speed of test and reduction in cost
The system must be responsive

- Define the capabilities
- Better availability of test results
- Streamline & develop evidence base
- Supportive regulatory structure
- Prioritise technologies
- Develop multiplex systems

System response
Diagnostics
– the signalling system for the NHS

• Direct patients and patient flows so that **the right people get to the right place at the right time**

• Ensure treatment and management is efficient, effective and coordinated

• Have a critical role in prioritising activity so that services are resilient and sustainable

• Fundamentally shape the health economics of particular patient pathways
The challenges of the commissioning landscape

- Commissioning landscape for diagnostics is complex and convoluted – with significant variation in location, contract form and performance information available.
- Provision models are ‘ad hoc’ and not always adherent with NICE guidance.
- Diagnostics can be ‘buried’ within other contracts – making it harder to commission for quality and consistency.
- Commissioners understanding of diagnostics can be poor with few templates for service specification.
- A lack of ‘line of sight’ between commissioners and providers makes it more challenging to structure and incentivise improvement activity and harder for quality providers to shape the market around them.
Driving action: incentives in the commissioning system

NHS England Incentive schemes to tackle AMR and improve safer care 2015-17 system wide

- 2 annual **Commissioner Quality Premiums** for improved antibiotic prescribing in primary care

The Quality Premium scheme is about rewarding Clinical Commissioning Groups for improvements in the quality of the services they commission. The scheme also incentivises CCGs to improve patient health outcomes and reduce inequalities in health outcomes and improve access to services.

- **Sepsis CQUIN** systematic screening for sepsis and timely treatment
- **AMR CQUIN** Reduced antibiotic consumption in acute trusts & improved stewardship review

The Commissioning for Quality and Innovation scheme is intended to deliver clinical quality improvements and drive transformational change. These will impact on reducing inequalities in access to services, the experiences of using them and the outcomes achieved.
Driving change: a RightCare approach through digital diagnostics

- Digitising diagnostic systems and sharing data will allow the comparability & analysis of diagnostic usage data.

- This will allow a RightCare approach providing comparisons with, for example, the PresQUIPP data providing information about antibiotic usage.
Personalisation – the future of care & management

Diagnostic & clinical information can be combined to better characterise individuals identifying underlying cause of their condition, so allowing better treatment selection.

Individually-tailored approach
- drugs
- devices
- interventions (e.g., surgery, radiotherapy)

Increasingly precision interventions based upon carefully identified subgroups within the broader population.

‘One size fits all’ treatments & intervention

- imaging
- established diagnostic tests - pathology, physiology etc
- next-gen diagnostic tests - genomic sequencing, biomarkers
- clinical records
- bioinformatic analysis
The power of diagnostics in AMR: opportunities and challenges

**Opportunities**

- Transforming existing pathways and approaches to support new models of care
- Unpicking commissioning of diagnostics to focus incentives
- Quality of data available about current use of diagnostics and outcomes
- Constant evolution of AMR requiring ongoing innovation to keep up

**Challenges**

- Next-gen diagnostics offer a precise, timely diagnosis – allowing the use of the right drug in the right place at the right time
- New settings for diagnostics allowing near-patient testing and greater use of other clan professionals (e.g., Pharmacy)
- Commissioning levers such as CQUIN, to drive uptake of new approaches
- Supporting screening and drug development programmes