Advances in Antimicrobial Stewardship (AMS) at University Hospital Southampton

Dr Julian Sutton
Consultant in Infectious Diseases & Medical Microbiology

Federation of Infection Societies
1st December, 2017
Disclosures

I have benefited from sponsorship to attend national and international meetings from Eumedica, Astellas and MSD.
Why is tackling antimicrobial resistance important?

**WHO IS PRESCRIBING?**

- **74%** General practice
- **11%** Hospital inpatients
- **7%** Hospital outpatients
- **5%** Dental practices
- **3%** Other community settings

**EUROPE**

- 25,000 people die each year as a result of hospital infections caused by 5 key resistant bacteria

**GLOBAL**

- A failure to address the problem of antibiotic resistance could result in:
  - 10m deaths by 2050
  - Costing £66 trillion
Background to the 2016/17 AMR CQUIN

- Total antibiotic consumption in English hospitals has been increasing steadily when adjusted for activity (admissions); rising by 6% between 2010 and 2014

- Piperacillin-tazobactam and carbapenems (mainly meropenem) consumption – rose much more sharply; by 62% and 42% in 5 years

- These increases in prescribing have coincided with increased antibiotic resistance
Piperacillin-tazobactam consumption
(ESPAUR report 2015)

Consumption of piperacillin-tazobactam in England

10.9% increase from 2013; 62% increase from 2010

Piperacillin/tazobactam supplied for UHS patients (all types) adjusted for admissions

Piperacillin-tazobactam: 10.9% increase 2015-16 vs 2013-14
Carbapenem consumption
(ESPAUR report 2015)

Consumption of carbapenem antibiotics in England

8.1% increase from 2013; 42% increase from 2010

Carbapenem antimicrobials supplied for UHS patients (all types) adjusted for admissions

Carbapenems: 9.7% increase 2015-16 vs 2013-14
The 2020 Goal: cut inappropriate prescribing of antibiotics by half

Speech
G7 2016 in Japan: PM press statement

Prime Minister David Cameron gave a press statement at the close of the G7 in Ise-Shima, Japan.

Good afternoon and welcome. Let me firstly start by saying it’s a real pleasure to be here. Japan is a beautiful country, and Ise-Shima is particularly breath-taking.

The G7 is a group of nations bound together by common values and common principles – freedom, democracy, the rule of law, a belief in open markets and respect for human rights.

But we need to go further. We need to act on both the demand for new antibiotics and the supply for existing ones.

And so we will cut inappropriate prescribing in the UK by half by 2020, leading the global field in reducing demand for antimicrobials.
The UK Government 5-year strategy

Published September 2013

7 key areas for future action:

1. Improving infection prevention and control
2. Optimising antibiotic prescribing
3. Improving professional education, training and public engagement
4. Developing new drugs, treatments and diagnostics
5. Better access to and use of surveillance data
6. Better identification and prioritisation of AMR research needs
7. Strengthened international collaboration
The NHS response

– A Quality Premium for CCGs for 2015-16 and 2016-17

– An AMR CQUIN for Acute Hospital Trusts for 2016-17
Primary Care: The Quality Premium

Expectations exceeded for 2015-16:

- Positive financial incentive for CCGs
- 2.7 million fewer antibiotics were prescribed compared to previous 12 months – 7.3% reduction
- 0.6 million fewer broad-spectrum items (co-amoxiclav, cephalosporins, ciprofloxacin) – a 15% reduction
Quality Premium impact: reduction in broad-spectrum prescriptions issued in the community

The number of broad-spectrum items reduced by 0.6 million items (15%) within the 12 months to a final value of **3,370,606** items in 12 months April15 – Mar16.
National CQUIN Goals 2016/17
(Commissioning for quality and innovation)

• Improving the health and wellbeing of NHS Staff

• Physical Health of People with Serious Mental illness (PSMI)

• Identification and Early Treatment of Sepsis

• Antimicrobial resistance (AMR)
5 AMR CQUIN Goals baseline year is 2013-14

1. Submission of ABx consumption data to PHE for years: 2014/15 to 2016/17

2. Reduction of 1% or more in total antibiotic consumption against the baseline* (5% reduction from last year required for UHS)

3. Reduction of 1% or more in carbapenem (mainly meropenem) against the baseline (11% reduction from last year required for UHS)

4. Reduction of 1% or more in piperacillin-tazobactam against the baseline (12% reduction from last year required for UHS)

5. Documented review within 72 hours in >90% ABx prescriptions
Defined daily doses of antibiotics dispensed by acute Trusts to inpatients and outpatients, per 1000 admissions, 2013-14

UHS 2013/14 total antibiotic consumption (treatment days per 1000 admissions)

Source: [http://fingertips.phe.org.uk/](http://fingertips.phe.org.uk/)
Accessed: 17 May 2016
DDD’s/100 admissions of piperacillin tazobactam dispensed by acute Trusts to inpatients and outpatients 2013-14

Source: http://fingertips.phe.org.uk/
Accessed: 17 May 2016
The UHS AMR CQUIN Group

- Face-to-face **teaching** – Junior Drs
- **Presentations** at Consultant meetings
- Ongoing antibiotic stewardship WRs
- Revision of Trust **Sepsis guidelines**
- **Email** to all UHS Consultants
- e-prescribing **course lengths** (e.g. “trimethoprim for 3 days”)
- Pre-72 hour **ABx review prompt** on Doctors’ Worklist
- Pharmacist-led audits of pre-72 hour ABx reviews
- Lobbied senior trust leaders for nursing/pharmacy/data analyst support
The UHS AMR CQUIN Group – further interventions

- Appointed a Band 6 nurse to a new **antimicrobial stewardship specialist** role to lead on nursing engagement with AMS

- Appointed a part time **data analyst** to support pharmacists in data surveillance and ABx consumption data submission to PHE

- **MicroGuide app updated** to reflect revised UHS sepsis guideline

- Revised Maternity services sepsis guidelines
- Revised CAP guidelines
- Publicity – WAAW, Info to CQC etc
Doctors’ Worklist alert icon to prompt review within 72 hours of starting antibiotics

<table>
<thead>
<tr>
<th>Ward / Bay / Bed / SR</th>
<th>Patient details</th>
<th>Diagnoses</th>
<th>Clinical Notes</th>
<th>Plan</th>
<th>Bloods</th>
<th>Chat jobs</th>
<th>Critical alerts</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS Isolation Ward (BDU)</td>
<td>Patient: NYM, J.</td>
<td>Primary: MERS</td>
<td>Working Diagnosis: Admitted overnight to CS ward</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bay: 10</td>
<td>Bed: 58</td>
<td>AKUT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consultant / Team</td>
<td>C. SUTTON, J (CR)</td>
<td>Secondary:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T. Infectious Disease</td>
<td></td>
<td>Comorbidities:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission/ECU data</td>
<td>Category</td>
<td>Worklist</td>
<td>Allergies</td>
<td>Issues</td>
<td>Jump To</td>
<td>Handover</td>
<td>Notes</td>
</tr>
<tr>
<td>Admission: 10/03/2016</td>
<td>Infectious Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **ABx** Patient has started antibiotics, review will be required in the next 48 hours.
- **ABx** 48 hours have elapsed since prescription and review must be completed.
- **ABx** Review has been completed and patient is still on antibiotics.
- **ABx** Review has been completed and patient is no longer on antibiotics.
Using e-prescribing to support appropriate durations

• New default options for oral antibiotics to encourage shorter course lengths and prompt patient review
Resistance in Gram-negative bacilli at UHS – all specimen types 2011-2015

There is resistance in less than 5% of Gram-negative bacilli specimens to pip-taz and a similar level of resistance to a combination of co-amoxiclav plus gentamicin.
2016: Revised UHS guideline for treatment of ‘sepsis’

- Emphasises prescribing by anatomical site
- For uncertain source of infection: 1st line regimen is a **combination of co-amoxiclav + gentamicin**

---

**FIRST LINE EMPIRICAL (BEST GUESS) TREATMENT OF RED FLAG SEPSIS & SEPTIC SHOCK IN ADULT INPATIENTS**

All patients require a review of any antibiotic therapy, for any indication, documented in the medical notes or electronically (e.g., on Doctor’s Worklist), within 24 hours of antibiotic therapy being started (i.e., by the end of day 0). The review may document decision to de-escalate or switch to PO therapy, (e.g., in response to Microbiology results or improved clinical status), or give reason for continuation of current antibiotic therapy, noting next antibiotic review or stop date.

### RED FLAG SEPSIS OF KNOWN SOURCE

- **E.g.** Respiratory tract, urinary tract, meningitis, bone/pelvis, chs, intra-abdominal, endocarditis/intravascular invasive line, Gastrointestinal

<table>
<thead>
<tr>
<th>NO PENICILLIN ALLERGY</th>
<th>NON-SEVERE PENICILLIN ALLERGY</th>
<th>SEVERE OR LIFE-THREATENING PENICILLIN-ALLERGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>If clear source of infection, follow organ-specific guideline for severe infection in MicroGuide app* (e.g., Body Systems &gt; Respiratory &gt; Pneumonia community-acquired severe) NOT the recommendations below for UNKNOWN source of sepsis.</td>
<td>If clear source of infection, follow organ-specific guideline for non-severe penicillin allergy in MicroGuide app* (e.g., Body Systems &gt; Respiratory &gt; Pneumonia community-acquired severe) NOT the recommendations below for UNKNOWN source of sepsis.</td>
<td>If clear source of infection, follow organ-specific guideline for severe infection for severe penicillin allergy in MicroGuide app* (e.g., Body Systems &gt; Respiratory &gt; Pneumonia community-acquired severe) NOT the recommendations below for UNKNOWN source of sepsis.</td>
</tr>
</tbody>
</table>

### RED FLAG SEPSIS OF UNKNOWN SOURCE

- Co-amoxiclav 1.25g IV 8-hourly (bolus over 3.5mins then flush with 10ml 0.9% sodium chloride) PLUS Gentamicin 3mg/kg IV bolus single dose (bolus over 3.5mins then flush with 10ml 0.9% sodium chloride) (Check MRSA status)
- Cefuroxime 1.5g IV 8-hourly PLUS Gentamicin 3mg/kg IV bolus single dose (Check MRSA status)
- Teicoplanin 50mg/kg (up to 800mg) IV 12-hourly for 3 doses then once-daily PLUS Gentamicin 3mg/kg IV bolus single dose (Check MRSA status)
- Piperacillin-tazobactam 4.5g IV 6-hourly PLUS Gentamicin 3mg/kg IV bolus single dose (Check MRSA status)
- Meropenem 500mg IV 6-hourly (Check MRSA status)
- Meropenem 500mg IV 6-hourly (If known MRSA sensitivity, contact Microbiology or O’Doctor)

**SEPTIC SHOCK**

- For BMI>30 patients, dose gentamicin on ideal body weight + 40% of excess weight. For other patients, use actual body weight.

*MicroGuide app for Android/Apple/Windows phones free to download. Desktop/laptop viewer link from Doctors Worklist Resources menu or at: [http://microguide.horizon.science](http://microguide.horizon.science)
The results
Total UHS Abx consumption reduced by 9% c/w 2013/14 (target 1% reduction)
UHS Pip-tazobactam consumption reduced by 26% c/w 2013/14 (target 1% reduction)
UHS Carbapenem consumption reduced by **24%** c/w 2013/14 (target 1% reduction)
90% of UHS patients had a documented ABx review within 72 hours in Q2, Q3 and Q4
Pneumonia at UHS: standardised mortality continues to fall

Relative Risk: 100% = predicted mortality for hospital case-mix
UTI at UHS: standardised mortality continues to fall

Relative Risk: 100% = predicted mortality for hospital case-mix
Septicaemia at UHS: standardised mortality continues to fall

Relative Risk: 100% = predicted mortality for hospital casemix
“In 2016, the commonest cause of bloodstream infections was *Escherichia coli*; of these, 41% were resistant to the commonest antibiotic used to treat infections in hospitals (co-amoxiclav) and almost one in five of these bacteria were resistant to at least one of other key antibiotics, though multi-drug resistance (resistance to three antibiotics) remained uncommon (<5%).

This suggests that patients with severe infections, including sepsis, who have risk factors for resistant bacteria, may require a combination of antibiotics, such as a β-lactam antibiotic and an aminoglycoside, for the first 24 hours of treatment while waiting for laboratory results to guide the choice of optimal therapy.”
UHS Abx consumption 2016/17 as AMR CQUIN interventions were introduced
The Abx escalation ‘escalator’
Percentage of UHS patients who receive a dose of ABx on any given day?

"Antimicrobial Stewardship is everyone’s business"

10%, 20%, 30%, 40%, 50%, 60%, 70%

‘YPOIs’
Young
Old
Pregnant
Immunocompromised (e.g. malignancy, immunosuppressants, biologics, etc)

Co-morbidities
Can we predict the future?
Simpsons “Bart to the Future” episode in 2000, predicts US presidency for Trump
Simpsons “Bart to the Future” episode in 2000, predicts US presidency for Trump
Proportion of Carbapenems Resistant (R+I) *Klebsiella pneumoniae* Isolates in 2010 and 2014
Multi-resistant pathogens in UHS (carbapenemase-producers)
To Conclude – UHS 20167/17 AMR CQUIN outcomes

A combination of novel AMS interventions from a committed multidisciplinary team, whilst continuing to do the basics well, led to very significant reductions in inappropriate prescribing of ultra-broad spectrum antibacterials, whilst maintaining safe patient care.

CQUIN itself - £668K
Savings on Abx in FY 2016/17 c/w previous FY - £240K
Overall ≈ £0.9M
Acknowledgments

Thankyou:
UHS AMR CQUIN Group
Kieran Hand & Hayley Wickens
Graeme Jones, Tatshing Yam, Sarah Glover, Sanjay Patel, Saul Faust, Patrick Lillie, Mike Vickers, Ian Jolliffe, Emily Bennett, many others

and all prescribers of ABx at UHS