Antimicrobial Stewardship in Humans
Dilip Nathwani; Ninewells Hospital and Medical School, Dundee, UK
Prevention & stewardship

Antimicrobial Use

INFLUENCERS:
• Human antimicrobial consumption
• Agriculture antimicrobial consumption

Infection Control

INFLUENCERS:
• Hand hygiene
• Epidemiology
• Outbreak investigations
• Cohorting
• Active surveillance

Environment

INFLUENCERS:
• Germicides
• 10% hypochlorite (sporicidal) for C. difficile
• Policy & Practice
  • What surfaces?
  • How often?
  • Is terminal enough? (NO!)

Susceptible organism
Resistant organism

*Antibiotics have a different propensity to select for resistance. For example, only a handful of high level resistant isolates of MRSA have become resistant to vancomycin in 4 decades of use. More MRSA strains have become resistant to daptomycin than to vancomycin in a single-clinical trial.
We have watched too passively as the treasury of drugs that has served us well has been stripped of its value. We urge our colleagues worldwide to take responsibility for the protection of this precious resource. There is no longer time for silence and complacency.
THE MULTI-DIMENSIONAL APPROACH

ANTIBIOTIC ECOSYSTEMS

Treatment & prophylaxis

Human medicine
Community
Hospital

Veterinary medicine

Animal feed additives

Agriculture

Plant protection

Environment
# A Sense of Perspective

<table>
<thead>
<tr>
<th>Type</th>
<th>Where used</th>
<th>Types of Use</th>
<th>Questionable use</th>
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<tbody>
<tr>
<td>Human (50%)</td>
<td></td>
<td>20% Hospital</td>
<td>20-50% unnecessary</td>
</tr>
<tr>
<td></td>
<td></td>
<td>80% Community</td>
<td></td>
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<tr>
<td>Animal (50%)</td>
<td></td>
<td>20% Therapeutic</td>
<td>40-80% highly questionable</td>
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<td>80% Prophylaxis/growth</td>
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<td>promotion</td>
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Wise *et al.* BMJ 1999; 317: 609-610
Outpatient Antibiotic Use

Total outpatient antibacterial use in the United States and 27 European countries in 2004

Retail sales of carbapenem antibiotics to treat Gram-negative bacteria are increasing rapidly in India and Pakistan.

Source: Based on data obtained under license from IMS Health MiDASTM (January 2005 - December 2010). IMS Health Incorporated. All Rights Reserved.
Non-prescription use occurred worldwide and accounted for 19–100% of antimicrobial use outside of northern Europe and North America.
Hospital Prescribing
National Point Prevalence Study 2009 (ESAC-3)
Scottish data

31 hospitals (8732 patients)
27.8% patients on antimicrobials
50.5% given intravenously
76.1% reason recorded in case notes
57.9% compliant with local guidelines
30.3% surgical prophylaxis more than one day

some room for improvement
OUTLINE OF PRESENTATION

• What is stewardship?
• “Structured guidance and support for responsible selection and utilization of antimicrobial agents”
OUTLINE OF PRESENTATION

• What is stewardship?
• Why stewardship?
THE TRIPLE AIMS OF STEWARDSHIP

• **1. IMPROVED PATIENT OUTCOMES**

An activity that **optimises antimicrobial management** and includes selection, dosing, route and duration of antimicrobial therapy and prophylaxis.

Also include clinical infection management and improving clinical outcomes: “beneficience”.

• **2. IMPROVED PATIENT SAFETY AND REDUCE RESISTANCE**

Selection of antimicrobials from each class of drugs that does the least harm through collateral damage e.g. MRSA, ESBLs, *C. difficile* and does not cause unintended harm [more complications, toxicity]: ”maleficience”

• **3. REDUCE COST**

ESGAP/ISC Global stewardship survey by continent

What continent are you from?

AMS Programme
- 78% yes
- 17% planned
- 5% don’t

Howard et al on behalf of ESGAP/ISC ECCMID 2013 Poster 2448
INTERVENTIONS TO IMPROVE ANTIBIOTIC PRESCRIBING IN HOSPITALS

- 89 STUDIES [till 2006]
- 55 FROM N. AMERICA; 37 EUROPE, 3 FAR EAST, 3 SOUTH AMERICA & 2 AUSTRALIA
- PERSUASIVE AND RESTRICTIVE INTERVENTIONS

- Davey P et al Cochrane systematic review
  Update April 30th 2013

- Evidence to support beneficial impact on:
  - Better quality of evidence and study design
  - Decrease in antibiotic use does not increase mortality and can improve clinical outcomes
  - Better use of antibiotics will reduce SSI’s
  - Decrease and better use of antibiotics reduces resistance and C. difficile
  - Emerging data on cost-reduction
Longevity of Value of Interventions

Mean and 95% CI; Restrictive – Persuasive [Davey et al Cochrane review update 2013]
450-bed district hospital in UK

1. **Restriction**: banning routine use of ceftriaxone and cipro (starting Aug 2008)
2. Plus **Educational campaign**

Outcomes:

1. **Cipro monthly consumption**: 72.5% reduction
   
   $109.8 \rightarrow 30.2$ DDD/1000 pt-occupied bed-days

2. **C. difficile reduction** of 77% (2.4 $\rightarrow$ 0.5 cases/1000 pt-bds)

3. **MRSA reduction** of 25% (1.2 $\rightarrow$ 0.9 cases/1000 pt-bds)
Outpt Israeli population (167,000 inhabitants) Nov 2001-May 2002
Intervention: RESTRICTION of cipro & preapproval
Outcome: reduction -1827.3 DDD/month (50% reduction in consumption)
Decreased cipro-R in E.coli isolates from urine by 36%
(12% \rightarrow 9%)
Post-intervention: back to previous situation
Impact of Stewardship on SAFETY?

The reductions in antimicrobial utilization associated with stewardship interventions have not been associated with any worsening in nosocomial infection rates, length of stay or mortality among intensive care patients.”

- “Stewardship interventions were associated with ... fewer antibiotic adverse events.”

COST V QUALITY BEFORE 2001-2004; DURING 2005-2008; AFTER 2009-2010

• MEASURES:
  • PRE-AUTHORISATION
  • GUIDELINES/POLICY WITH ADHERENCE
  • DISCONTINUE UNECESSARY DOUBLE COVERAGE
  • IV-ORAL
  • ID CONSULT FOR COMPLEX CASES
  • 45.5% DECREASE IN ANTIMICROBIAL COSTS
  • QUALITY: NO INCREASE IN MORTALITY, READMISSIONS AND LOS
  • POST STEWARDSHIP PROGRAMME LED TO 32.3% INCREASE IN COSTS IN 2 YEARS
OUTLINE OF PRESENTATION

• How stewardship? Emphasis on implementation
Linked aims of improvement

Better patient (and population) outcomes

Better professional development

Everyone

Better system performance

Antibiotic Stewardship
Essential: All Healthcare facilities
A PATIENT SAFETY PRIORITY

• Clear vision with aims, objectives and measurables [identify quick wins, focus] – identify benefits to all key stakeholders – consider the patient voice
• Organisational and clinical leadership, accountability, structure and organisation [networks of support - local, regional and national]
• Operational multi-disciplinary stewardship team with clinician champion; important role of pharmacists and nurses
• Key effective intervention tools adopted for local needs, geography, organisation and resource [key is to reduce diagnostic uncertainty]
• Multi-faceted implementation efforts: improvement science, socio-behavioural methods, human factors
• Measurement [improvement v scrutiny], external inspection, feedback
• Education: BETTER LEARNING = BETTER CARE face to face, e-learning, reflective learning in the workplace
• Communication
Driver Diagram for Antimicrobial stewardship

Structure + Process = Outcome

Quality of healthcare can be assessed on the basis of structure, process (how care is delivered), and outcome (mortality, functional status, quality of life, and patient satisfaction).

Good measures of the first two are those that have a clear relationship to the third.

Structure must proceed process which must proceed outcome.
Organisational Approach required

- Addressing AS as an organisational change issue need to consider:
  - Issues and agendas: Political science concept of a crowded decision making agenda;
  - Power and influence: Specialists and generalists, Who ‘owns’ antibiotic stewardship? Coalition building needs?
  - Governance framework
  - Roles and relationships: difficult move from a narrow technical role to a broader strategic role, coalition of supporters
  - Organisational culture and learning
  - Supporting Knowledge bases

- E Ferlie et al 2003 British Journal of Management, 14, S1: S1-14. courtesy of a.holmes
IMPORTANCE OF COMBINING INFECTION PREVENTION AND ANTIMICROBIAL STEWARDSHIP

Valiquette L et al. CID 2007; 45, S112-S121.
Organisational memory and role of nurses in stewardship

- Prescribing most commonly performed by junior doctors
- Outside area of expertise with varying levels of senior support
- High rotation of junior doctors
- Loss of local knowledge
- Antibiotic prescribing sits outside one specialty
- However, nurses can contribute to this local knowledge as the least transient population

INTEGRATED NETWORKS
Evidence based interventions including Antibiotic Stewardship program in Vietnamese hospitals.

1. Indicators
   - antibiotic use,
   - resistance,
   - health care associated infections
   - infection control
2. Improved Susceptibility Testing
3. Antibiotic Stewardship groups 16 hospitals

Courtesy of H. Hanberger
Antimicrobial Stewardship Toolkit:

Quality of Evidence to support interventions

• Prospective audit with intervention and feedback AI
• Education BIII [Education with an active intervention AIII]
• Formulary restriction and pre-authorisation
  All for rapid decrease in antibiotic in use
  BII for control of outbreak
  BII/III may lead to unintended increase in resistance
• Guidelines and clinical pathways AII
  – With education and feedback on outcomes AIII
• Antimicrobial cycling CII
• Antimicrobial order forms BII
• Combination therapies CII
  – In critically unwell patient with high risk of MDRO AII
• De-escalation-review AII
• Dose optimisation AII
• Parenteral to oral conversion AIII
• Computerised decision support, surveillance BII
• Laboratory surveillance and feedback BII

Adapted from Dellit et al. Clinical Infectious Diseases 2007; 44:159-77
General workflow schematic for a two-step prospective audit and feedback strategy as well as formulary restriction and preauthorization strategy for antimicrobial stewardship.

Chung GW et al. Antimicrobial stewardship: A review of prospective audit and feedback systems and an objective evaluation of outcomes
“Low Hanging fruit” [LARGE EFFECT BUT LOW COST] as Antimicrobial Stewardship Initiatives

• GENERAL
  • IV-ORAL CONVERSION
  • THERAPEUTIC SUBSTITUTION
  • BACTCHING IV ANTIMICROBIALS

• FORMULARY RESTRICTIONS
  • SINGLE DOSE SURGICAL PROPHYLAXIS
  • DURATION OF VANCOMYCIN AND AMINOGLYCOSIDES

Adapted from Goff DA et al CID 2012; 55(4): 587-92
Morris AM et al Healthcare Quality 2010; 13(2): 64-70
Policies and guidelines are not enough….

J Carthey et al BMJ 2011; 343
THE IMPLEMENTATION GAP

17 years to apply 14% of research knowledge to patient care!

“Think and work smarter-Improvement science”

Balas EA, Boren SA. Managing clinical knowledge for health care improvement. Yrbk of Med Informatics 2000; 65-70
Right drug, right time, right dose & right duration

- **Start smart**
  - initiate effectively antibiotic **ASAP** for serious infections
  - send appropriate specimens prior to starting treatment
  - use local and national guidance
  - document in notes
  - shortest course
  - choose narrow spectrum with least ecological damage
  - TDM when relevant to reduce toxicity e.g. aminoglycosides
  - single dose for surgical prophylaxis

- **Then Focus**
  - at 48-72 hours review
  - stop if no infection
  - streamline according to micro results
  - iv to oral switch
ANTIBIOTIC CARE
“BUNDLES”

On initiation of prescription:
1. Clinical rationale for initiation
2. Appropriate specimens sent for MC&S
3. Adherence to local prescribing guidelines
4. Additional clinical interventions to manage infection (e.g., remove indwelling device, surgical procedure)

On continuation of prescription:
1. Daily review based on clinical response and laboratory results regarding: De-escalation, IV to Oral switch, Stopping
2. Correct therapeutic drug monitoring

Toth NR, Chambers RM, Davis SL. Am J Health Syst Pharm. 2010 May 1;67(9):746-9.
Review Bundle: The effect of Force and Function

- The 3 Day Antibiotic Bundle

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<th>Time</th>
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<td>18</td>
</tr>
<tr>
<td>Pharmacy</td>
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**INDICATION: Empirical Treatment**
- Start Date: 1/15
- Review Date: 2/22

**Action Taken on Review**
- Check Central Vision for Results
- Review patient & initial diagnosis
- Consider IV to Oral Switch
RAPID DIAGNOSTICS & BIOMARKERS

Flow diagram for incorporating PCT into clinical practice. Diagnostic criteria and treatment recommendations as per appropriate guidelines.76–78.


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Changing behaviour?

Antibiotic prescribing in hospitals: a social and behavioural scientific approach

Marlies EJL Hulscher, Richard P TM Grol, Jos W M van der Meer

Panel: Examples of potentially effective strategies to improve antibiotic use in hospitals

Improvement strategies at the organisational level

Antibiotic policies
- Provide an antibiotic formulary
- Provide an antibiotic order form
- Provide an antibiotic order form including restriction requiring prior authorisation of prescriptions by infectious disease physicians, microbiologists, pharmacists
- Provide automatic stop orders
- Install an infection prevention committee
- Provide written antibiotic guidelines
- Provide an antibiotic booklet

Strategies to improve coordination, collaboration, communication, teamwork, and care logistics
- Introduce pharmacists to review orders and to contact physicians to reinforce appropriate use
- Introduce ward rounds to stimulate collaboration between doctor and pharmacist or microbiologist
- Introduce telephone advice for doctors to discuss prescriptions with the pharmacist or microbiologist
- Introduce flowsheets regarding the coordination of care
- Improve the logistics of care, for example, to reduce the time between requesting laboratory diagnostics and prescribing antibiotics

Improvement strategies at the individual level

- Distribute educational materials (e.g., guidelines)
- Provide group education including conferences, seminars, and skills training programmes
- Provide small group education
- Stimulate local consensus processes
- Use local opinion leaders
- Provide individual instruction at the physician’s office (outreach visits or academic detailing)
- Provide feedback (provision of summary of clinical performance, based on, for example, medical records)
- Provide reminders (prompts to perform specific actions), including decision support by computer

But – remember, not all prescribers are equal or equivalent…
Greater Understanding Antimicrobial Prescribing Behaviours

Understanding the Determinants of Antimicrobial Prescribing within hospitals: The role of ‘Prescribing Etiquette’

1. Non-interference with the prescribing decisions of colleagues: Reluctance to interfere with the prescribing decisions of colleagues. In the case of antimicrobial prescribing there is a reluctance to intercept antimicrobial prescriptions started by colleagues. This recognises the autonomous decision making process of prescribing.

2. Accepted non-compliance to policy: Deviations from policy recommendations are tolerated and put in the context of the prescriber’s experience, expertise and the specific clinical scenario. This leads to hierarchy and expertise, and not policy as determinants of prescribing practice behaviours.

3. Hierarchy of prescribing: Prescribing as an activity is performed by junior doctors. But it is the senior doctors who decide what is prescribed.
Measuring Impact of a stewardship programme: success or failure
Integrating the Three Faces of Performance Measurement

The three faces of performance measurement should not be seen as mutually exclusive silos. This is not an either/or situation.

All three areas must be understood as a system. Individuals need to build skills in all three areas.

Organizations need translators who and be able to speak the language of each approach.

The problem is that individuals identify with one of the approaches and dismiss the value of the other two.

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We are increasingly realizing not only how critical measurement is to the quality improvement we seek but also how counterproductive it can be to mix measurement for accountability or research with measurement for improvement.

Performance Measures and Measurement

The Three Faces of Performance Measurement:
Improvement, Accountability, and Research

Leif J. Solberg, MD
Gordon Mosser, MD
Sharon McDonald, RN, PhD
Data for Improvement

Using Data to understand progress toward the team’s aim

Using Data to answer the questions posed on in the plan for each PDSA cycle
Antibiotic Measures: Process, Outcomes and Balancing

**PROCESS**

Amount of antibiotic in DDD/100 bed days
- Promoted antibiotic
- Restricted antibiotics

Compliance with acute empiric guidance – documentation in notes and compliance with policy

Compliance with surgical prophylaxis – < 60 min from incision, < 24 hours and compliance with local policy

Compliance with “other bundles” – all or nothing [3 Day antibiotic review bundle, VAP, CAP bundle’ s]

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**Outcome measures**
- CDI rates
- SSI rates
- Surveillance of resistance
- Mortality [SMR’ s]

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**Balancing measures** [unintended consequences]
- Mortality
- SSI’ s
- Readmissions to hospital within 30 days of discharge
- Admissions to ICU
- Rate of complications
- Treatment related toxicity - e.g aminoglycoside related toxicity
DEVELOPMENT OF QUALITY METRICS FOR ASP’S THROUGH A MODIFIED DELPHI TECHNIQUE
ICHE 2012; 33[3]: 500-506

- **ANTIMICROBIAL CONSUMPTION MEASURES**
  - Days of therapy per 1000 patient day
- **ANTIMICROBIAL RESISTANCE MEASURES**
  - No of patients with specific drug resistant organism/total number of patients admitted to ward/unit

- **PATIENT OUTCOME MEASURES**
  - Mortality related to AR pathogens
  - Conservable days of therapy among CAP,SSTI,BSI & sepsis
  - Unplanned hospital readmission within 30 days after hospital discharge

**ACCOUNTABILITY MEASURES/PUBLIC REPORTING**
**TARGETS WITH AUDIT AND FEEDBACK**

**QI MEASURES/INTERNAL USE**
2012 theory-based Cochrane review of Audit & Feedback

- Median 4.3% increase in compliance (IQR 0.5% to 16%)
- A&F is more effective when combined with
  - Explicit targets and an action plan
- In addition,
  - the target was prescribing
  - the source was a supervisor or colleague
  - it was provided more than once
  - it was delivered in both verbal and written formats
GLOBAL STEWARDSHIP SURVEY
2012: Barrier’ s: ESGAP/ICC
Howard P, Nathwani D et al ECCMID 2013, POSTER 2448

Barriers to providing a planned AMS Programme

- Lack of funding/people (Planned ASP)
- Higher priorities (Planned ASP)
- Admin not aware (Planned ASP)
- Prescriber opposition (Planned ASP)
- Lack of IT (Planned ASP)
- No barriers (Planned ASP)
SOLUTIONS TO BARRIER’S

• Funding/personnel shortage: Team working, single & shared budget, targeted ASP’s & ICT’s are cost-effective
• Higher priority initiatives: AMR & Prescribing a patient safety priority, use patient stories and political leverage, senior leadership /champions
• Opposition for prescribers: concentrate on improving patient outcomes without harm; show “quick wins” to get rapid engagement
• Administrator reluctance: engage them in safety and cost consequences of AMR; involve senior and middle managers
• IT: do simple & most meaningful measurement; paper first; road [testing] before technology
THANK YOU
dilip.nathwani@nhs.net