HUMAN ANTIMICROBIAL STEWARDSHIP: PRESERVING CURRENT AND FUTURE ANTIMICROBIALS

ONE HEALTH 2018

Dilip Nathwani
Antibiotic resistance is the quintessential One Health issue

A European One Health Action Plan against Antimicrobial Resistance (AMR)

One Health: is a term used to describe a principle which recognises that human and animal health are interconnected, that diseases are transmitted from humans to animals and vice versa and must therefore be tackled in both. The One Health approach also encompasses the environment, another link between humans and animals and likewise a potential source of new resistant microorganisms. This term is globally recognised, having been widely used in the EU and in the 2016 United Nations Political Declaration on AMR.
WHY ARE WE TARGETING ANTIMICROBIAL PRESCRIBING?
“ANTIMICROBIAL USE IS THE KEY DRIVER OF RESISTANCE. THIS SELECTIVE PRESSURE COMES FROM A COMBINATION OF OVERUSE... AND ALSO FROM MISUSE”
Antimicrobial stewardship has been defined as “the optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance.”

**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’.

![Diagram](image.png)

*Figure 1. The 4Ds of antimicrobial therapy: the right Drug, Dose, Duration and De-Escalation.*
Global antibiotic consumption by country income classification: 2000–2015

Eili Y. Klein et al. PNAS doi:10.1073/pnas.1717295115
Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis

Peter Collignon, John Jorga, Timothy R Walsh, Sunanth Gandra, Kumanan Lanmanarupan

Interpretation Reduction of antibiotic consumption will not be sufficient to control antimicrobial resistance because contagion—the spread of resistant strains and resistance genes—seems to be the dominant contributing factor. Improving sanitation, increasing access to clean water, and ensuring good governance, as well as increasing public health care expenditure and better regulating the private health sector are all necessary to reduce global antimicrobial resistance.

| GDP per capita index (standardised) | 3.36 | 0.11 |
| Education index | 8.59 | 0.0035 |
| Infrastructure index | -13.24 | 0.0052 |
| Climate index | -0.25 | 0.86 |
| $R^2$ | 0.75 | |

GDP = gross domestic product. $R^2$ = coefficient of determination.

Table 3: Effect of changes in indices on the aggregate resistance rate

Lancet Planet Health 2018; 2: e398-405
Figure 5. Consumption of antibiotics for systemic use in the hospital sector by antibiotic group, EU/EEA countries, 2016 (at ATC group level 3, expressed as DDD per 1 000 inhabitants per day).

(a) Finland: data include consumption in remote primary healthcare centres and nursing homes.
(b) Portugal: data relate to public hospitals only.

EU/EEA refers to the corresponding population-weighted mean consumption based on 23 countries that provided data.
A SENSE OF PERSPECTIVE

WHERE USED

HUMAN: 50%
ANIMAL: 50%

TYPES OF USE

COMMUNITY: 80%
PROPHYLAXIS/GROWTH PROMOTION: 80%
THERAPEUTIC: 20%
HOSPITAL: 20%

QUESTIONABLE USE

AMS: ~80% in hospitals
20% in community

EU SURVEY

20-50% UNNECESSARY
40-80% HIGHLY QUESTIONABLE

Wise et al. BMJ 1999; 317: 609-610
EVIDENCE FOR AMS EFFECTIVENESS
Authors' conclusions:

We found high-certainty evidence that interventions are effective in increasing compliance with antibiotic policy and reducing duration of antibiotic treatment. Lower use of antibiotics probably does not increase mortality and likely reduces length of stay. Additional trials comparing antibiotic stewardship with no intervention are unlikely to change our conclusions. Enablement consistently increased the effect of interventions, including those with a restrictive component. Although feedback further increased intervention effect, it was used in only a minority of enabling interventions. Interventions were successful in safely reducing unnecessary antibiotic use in hospitals, despite the fact that the majority did not use the most effective behaviour change techniques. Consequently, effective dissemination of our findings could have considerable health service and policy impact. Future research should instead focus on targeting treatment and assessing other measures of patient safety, assess different stewardship interventions, and explore the barriers and facilitators to implementation. More research is required on unintended consequences of restrictive interventions.
Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and *Clostridium difficile* infection: a systematic review and meta-analysis

**Table:**

<table>
<thead>
<tr>
<th>MDR GNB</th>
<th>Events/patient-days Before</th>
<th>Events/patient-days After</th>
<th>Incidence ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apisarnthanarak et al.²³</td>
<td>13/2889</td>
<td>1/1324</td>
<td>0.08 (0.00–1.41)</td>
</tr>
<tr>
<td>Marra et al.²³</td>
<td>23/8421</td>
<td>2/8066</td>
<td>0.09 (0.02–0.39)</td>
</tr>
<tr>
<td>Agisarnthanarak et al.²³</td>
<td>33/2889</td>
<td>31/324</td>
<td>0.13 (0.03–0.55)</td>
</tr>
<tr>
<td>Tement et al.²³</td>
<td>27/698794</td>
<td>6/635794</td>
<td>0.24 (0.10–0.50)</td>
</tr>
<tr>
<td>Cook and Gooch²⁷</td>
<td>44/220474</td>
<td>13/261318</td>
<td>0.25 (0.13–0.46)</td>
</tr>
<tr>
<td>Peto et al.²⁷</td>
<td>24280</td>
<td>1/4217</td>
<td>0.25 (0.01–5.63)</td>
</tr>
<tr>
<td>Takesue et al.²⁷</td>
<td>39/698794</td>
<td>10/635794</td>
<td>0.28 (0.14–0.58)</td>
</tr>
<tr>
<td>Arda et al.²⁶</td>
<td>39/698794</td>
<td>10/635794</td>
<td>0.33 (0.16–0.68)</td>
</tr>
<tr>
<td>Leveiller-van Hall et al.²⁵</td>
<td>28/285606</td>
<td>10/308852</td>
<td>0.36 (0.11–1.47)</td>
</tr>
<tr>
<td>Yeo et al.²³</td>
<td>10/19142</td>
<td>4/23589</td>
<td>0.44 (0.19–1.02)</td>
</tr>
<tr>
<td>Arnaud et al.²³</td>
<td>8/285606</td>
<td>8/21798</td>
<td>0.46 (0.14–1.54)</td>
</tr>
<tr>
<td>Marra et al.²³</td>
<td>6/8421</td>
<td>3/8066</td>
<td>0.52 (0.13–2.99)</td>
</tr>
<tr>
<td>Arda et al.²⁶</td>
<td>15/8421</td>
<td>8/8066</td>
<td>0.56 (0.24–1.31)</td>
</tr>
<tr>
<td>Meyer et al.²⁴</td>
<td>45/285606</td>
<td>29/308852</td>
<td>0.60 (0.37–0.95)</td>
</tr>
<tr>
<td>Imipenem-resistant A baumannii</td>
<td>34/13502</td>
<td>33/21420</td>
<td>0.61 (0.38–0.99)</td>
</tr>
<tr>
<td>Imipenem-resistant P aeruginosa</td>
<td>10/20469</td>
<td>9/21798</td>
<td>0.85 (0.34–2.08)</td>
</tr>
<tr>
<td>Zou et al.²⁷</td>
<td>185/834560</td>
<td>172/883500</td>
<td>0.88 (0.71–1.08)</td>
</tr>
<tr>
<td>Nwia et al.²⁵</td>
<td>11/128146</td>
<td>15/113873</td>
<td>1.53 (0.70–3.34)</td>
</tr>
<tr>
<td>Aubert et al.²⁷</td>
<td>49/5100</td>
<td>44/2548</td>
<td>1.80 (1.29–2.70)</td>
</tr>
</tbody>
</table>

**Figure 2:** Forest plot of the incidence ratios for studies of the effect of antibiotic stewardship on the incidence of MDR GNB. GNB = Gram-negative bacteria. MDR = multidrug-resistant. XDR = extensively drug-resistant.
**SYSTEMATIC REVIEW AND META-ANALYSIS: IMPACT OF KEY TECHNICAL INTERVENTIONS**

- **Adherence to local guidelines**
  - Mortality: RRR 35% [RR 0.65, 95% CI 0.54–0.8; P<0.0001]
- **Culture driven de-escalation**
  - Mortality: RRR 65% [RR 0.44, 95% CI 0.3–0.66; P<0.0001]
- **S.aureus bacteraemia clinical review**
  - Mortality: RRR 66% [RR 0.34, 95% CI 0.25–0.75; P<0.008]
- IVOST No difference in mortality? Reduced LOS
- Restriction of antibiotics decreased consumption and in many studies resistance to the drug-bug profile
- TDM decreased nephrotoxicity

Growing evidence from all sectors

A Systematic Review of Antimicrobial Stewardship Interventions in the Emergency Department

Mia Losier¹, Tasha D. Ramsey, PharmD¹,², Kyle John Wilby, PharmD¹, and Emily K. Black, PharmD¹

Interventions to improve antibiotic prescribing practices in ambulatory care (Review)

Arnold SR, Straus SE

Antibiotic stewardship interventions in hospitals in low-and middle-income countries: a systematic review

Christophe Van Dijck, Erika Vlieghe & Janneke Arnoldine Cox

EVIDENCE-BASED CHILD HEALTH: A COCHRANE REVIEW JOURNAL
Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/ebch.23

Journal of the American Medical Directors Association
Volume 19, Issue 2, February 2018, Pages 110-116

Review Article
Antibiotic Stewardship Programs in Nursing Homes: A Systematic Review

Diana Feldstein MD, MPH ¹,²,³, B. Philip O. Raas MD, MPH ¹, Pendalyn C. Hickey, MPH ¹,²,³, Cynthia Feltner MD, MPH ¹,²,³

¹ Division of Geriatric Medicine, Center for Aging and Health, University of North Carolina, Chapel Hill, NC
² Department of Family Medicine, University of North Carolina, Chapel Hill, NC
³ Cecil G. Sheps Center for Health Services Research, University of North Carolina, Chapel Hill, NC

A total of 14 studies rated good or fair quality were included. Eight studies reported a reduction in antibiotic prescriptions. Ten found an increase in adherence to guidelines proposed by the studied ASP. None reported a statistically significant change in NH mortality rates, C. difficile infection rates, or hospitalizations.

Discussion
The limited research to date suggests that NH ASPs can affect intermediate health outcomes, but not key health outcomes or health care utilization.

Conclusion
Larger trials evaluating more intensive interventions over longer durations may be needed to determine whether ASPs in NHs improve health outcomes as they have in hospitals.
EVIDENCE FOR AMS ACROSS HEALTH SYSTEMS, RESOURCE SETTINGS

We still need more evidence of what works where, for how long and why?

However in the meantime .......

Table 1
Recommended resources for design and reporting of antimicrobial stewardship interventional studies

Design of interventional study
- Recommended designs: randomized, cluster-randomized trials and controlled interrupted time series quasi-experimental studies [7,15].
- Use implementation science to design intervention, which should be tailored to (evaluation of) existing barriers and facilitators [7,15,16].
- Assess impact of intervention on balanced set of a priori-defined and relevant criteria [7,15–17].
  - Process measures (e.g., uptake of intervention).
  - Outcome measures (e.g., antibiotic use, resistance, clinical outcomes).
  - Unintended consequences.
  - Economic evaluation if possible [18].
- Sustainability of medium- to long-term impact of intervention should be monitored.
WHAT IS BEING IMPLEMENTED- HUMAN AMS

JUST DO IT.
Optimizing the use of antimicrobial medicines in human and animal health (Global Action Plan Objective 4)

Progress in the global response to antimicrobial resistance has been largely driven by national action plans, which are designed to preserve antimicrobial effectiveness [5,11]. The second wave of this national self-assessment survey shows that there has been some action on this front, but there is also substantial room for improvement. For example, 123 countries (79.9%) have policies in place to regulate the sale of antimicrobials, including the requirement of a prescription for human use, which is a policy that has been shown to be effective in reducing antimicrobial use in some parts of the world [12,13]. Yet these policies are less common in low-income countries, where only 52.6% of countries (n=10) have these policies. 102 countries (66.2%) have policies to optimize antimicrobial use at Level 3 or higher; however, only 7 countries globally have reached Level 5 and are systematically sending data back to prescribers, another policy shown to reduce antimicrobial prescribing among physicians [14]. However, 26.6% of responding countries (n=41) have guidelines in place to enable appropriate use of antimicrobials or optimize antibiotic use (Level 4–5) in human health facilities.
WE HAVE JUST HEARD SIMILAR RESULTS FROM EUROPEAN SURVEY – KACELNIK ET AL
“Society’s huge investment in technological innovations that only modestly improve efficacy, by consuming resources needed for improved delivery of care, may cost more lives than it saves.”

“Health, economic, and moral arguments make the case for spending less on technological advances and more on improving systems for delivering care.”
AMS IN HUMAN IS A WHOLE SYSTEMS APPROACH: DOING AMS IN ISOLATION IN ONE COMPONENT OF THE SYSTEM WILL NOT BE SUCCESSFUL IN THE LONG TERM
Managing responsible antimicrobial use: perspectives across the healthcare system

Clinical Microbiology and Infection 23 (2017) 441–447

O.J. Dyar 1,4, G. Tebano 2,4, C. Pucini 3,4, on behalf of ESCAP (ESCMID Study Group for Antimicrobial stewardship)

**Example of One system Approach**

**Hospital**

**LTCF**

**Primary care**

**Others**

**Key features of Strama**

*Grounded in daily practice:* Face-to-face visits at primary care practices are commonly carried out within regions. These allow feedback of data to prescribers and encourage prescribers to share their perceived barriers to responsible antibiotic use.

*Regional autonomy:* The decentralized organization of Strama has stimulated local goal setting and local piloting of improvement measures, accepting that there are multiple paths to the shared goal.

*Multidisciplinary at each level:* The regional Strama groups are led by a county medical officer (usually an infectious diseases doctor), and always contain specialists in primary care, clinical microbiology, infectious diseases, ear nose and throat, and paediatrics, together with pharmacists and representation from the local drug and therapeutics committee. Nurses and dentists are included in some regional groups. The national level Strama council involves clinical representation that mirrors the regional groups, and cooperates with 20 authorities across public health, animal health, food, and the environment, in part through an intersectoral coordinating mechanism introduced in 2012.

*Data-driven:* Data collection and analyses are coordinated and standardized, resulting in robust datasets for monitoring antibiotic use and resistance at national level, and for providing high resolution feedback at regional levels. Data collection has even included monitoring for adverse events of under-prescribing. IT systems are now being developed in many counties to provide individual prescriber feedback, including comparisons with local colleagues.
An international cross-sectional survey of antimicrobial stewardship programmes in hospitals

P. Howard\textsuperscript{a}, C. Pulcini\textsuperscript{2,3}, G. Levy Harr\textsuperscript{4}, R. M. West\textsuperscript{5}, I. M. Gould\textsuperscript{6}, S. Harbarth\textsuperscript{7} and D. Nathwani\textsuperscript{2} on behalf of the ESCMID Study Group for Antimicrobial Policies (ESGAP) and ISC Group on Antimicrobial Stewardship

\textit{J Antimicrob Chemother} 2015; 70: 1245 – 1255

Figure 1. Barriers to delivering a functional and effective AMS programme.
Quality Assessment

Donabedian’s Structure – Process - Outcome

Antecedents → Structure → Process → Outcome

Factors that can influence structure, process:
- Environmental factors
- Patient factors (also influence outcomes)

Organizational characteristics

Interactions between healthcare practitioner & patient

Changes (desirable or undesirable) in individuals & populations

Organizational Attributes (“Structure”)
- Physical characteristics
- Management
  - Executive leadership
  - Board responsibilities
- Culture
  - Organizational design
  - Information management
  - Incentives

Process
- Diagnosis
- Treatment

Outcomes
- Morbidity
- Mortality
- Service quality

Facilitators and barriers to implementing antimicrobial stewardship strategies: Results from a qualitative study

Fig 1. Factors related to implementation of antimicrobial stewardship program strategies.
The Need to Study Implementation

On average, it takes 17 years for evidence-based practices to be incorporated into routine care.

Efficacy and effectiveness trials → Lack of awareness
Competing demands
Limited resources and skills
Misalignment of priorities

Sustained application in routine care


Strategy, Leadership, Organisation & Systems and Resources

Structure \([Sc]\) + Process \([Pi]\) = Outcomes \([Od]\)
Core elements:

1. Senior hospital management leadership towards AMS
2. Accountabilities and responsibilities
3. Available expertise on infection management
4. Education and practical training
5. Other actions aiming at responsible antimicrobial use
6. Monitoring and surveillance (on a continuous basis)
7. Reporting and feedback (on a continuous basis)
Antibiotic stewardship programs (ASPs) improve antibiotic prescribing. Seventy-three percent of US hospitals have <200 beds. Small hospitals (<200 beds) have similar rates of antibiotic prescribing compared to large hospitals, but the majority of small hospitals lack ASPs that satisfy the Centers for Disease Control and Prevention’s core elements. All hospitals, regardless of size, are now required to have ASPs by The Joint Commission, and the Centers for Medicare and Medicaid Services has proposed a similar requirement. Very few studies have described the successful implementation of ASPs in small hospitals. We describe barriers commonly encountered in small hospitals when constructing an antibiotic stewardship team, obtaining appropriate metrics of antibiotic prescribing, implementing antibiotic stewardship interventions, obtaining financial resources, and utilizing the microbiology laboratory. We propose potential solutions that tailor stewardship activities to the needs of the facility and the resources typically available.

**Keywords.** antibiotic stewardship; small community hospital; antibiotic prescribing appropriateness.
A pilot study using telehealth to implement antimicrobial stewardship at two rural Veterans Affairs medical centers

Table 3. Roles of VAST Participants Who Attended at Least 1 Session During the 1-Year Study Period

<table>
<thead>
<tr>
<th>Role</th>
<th>Site A</th>
<th>Site B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention site</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Infection preventionists</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Nurses</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Nurse practitioners and physician assistants</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Pharmacists</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Physicians</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Trainees</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Remote site</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Infectious diseases physicians</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Research team members</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Information technologist</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: VAST, videoconference antimicrobial stewardship team.

Table 2. Recommendations Made by the VAST and Accepted by Primary Team

<table>
<thead>
<tr>
<th>Recommendations, No. Accepted of Those Made (%)</th>
<th>Site A</th>
<th>Site B</th>
</tr>
</thead>
<tbody>
<tr>
<td>All recommendations</td>
<td>106/256 (73)</td>
<td>94/153 (66)</td>
</tr>
<tr>
<td>Recommendations about antibiotics</td>
<td>111/167 (61)</td>
<td>124/154 (78)</td>
</tr>
<tr>
<td>Stop antibiotic(s)</td>
<td>54/66 (82)</td>
<td>32/45 (71)</td>
</tr>
<tr>
<td>Continue antibiotic(s)</td>
<td>58/31 (90)</td>
<td>5/6 (83)</td>
</tr>
<tr>
<td>Change antibiotic agent, dose or length of therapy</td>
<td>15/25 (60)</td>
<td>22/40 (55)</td>
</tr>
<tr>
<td>Start new antibiotic</td>
<td>9/10 (90)</td>
<td>7/7 (100)</td>
</tr>
<tr>
<td>Do not start or renew antibiotic</td>
<td>5/5 (100)</td>
<td>6/6 (100)</td>
</tr>
<tr>
<td>Other recommendations</td>
<td>83/119 (68)</td>
<td>27/49 (55)</td>
</tr>
<tr>
<td>Diagnostic imaging or labs</td>
<td>35/48 (73)</td>
<td>12/18 (67)</td>
</tr>
<tr>
<td>Obtain consult</td>
<td>15/25 (60)</td>
<td>7/4 (50)</td>
</tr>
<tr>
<td>Nonpharmacologic intervention (e.g., wound care, change urinary catheter)</td>
<td>8/18 (44)</td>
<td>4/7 (57)</td>
</tr>
<tr>
<td>Further evaluation pending results of diagnostics tests or other records</td>
<td>8/9 (89)</td>
<td>...</td>
</tr>
<tr>
<td>Education to patient and/or caregivers</td>
<td>4/5 (80)</td>
<td>...</td>
</tr>
<tr>
<td>Start or stop medication other than an antibiotic</td>
<td>3/4 (75)</td>
<td>4/6 (67)</td>
</tr>
<tr>
<td>Other*</td>
<td>8/10 (80)</td>
<td>0/4 (0)</td>
</tr>
</tbody>
</table>
Figure 1: Hub and spoke model

Legend:
- Central Site = Mount Sinai University Health Network Antimicrobial Stewardship Program
- Hub Site Lead = Hub Lead Hospital
- Spoke Site = Community Hospital
Antibiolor, the Lorraine antibiology network: Update on 7 years of activity

4. Network tasks undertaken to reach previously mentioned objectives

4.1. Writing out guidelines

4.2. Evaluation of professional practice

4.3. Continuous education actions

4.3.1. An information letter: “Antibiolor Infos”

4.3.2. Peer visits

4.5. Telephone advice for antibiotic therapy

4.6. Collection and analysis of microbiological data on bacterial resistance and of the antibiotic consumption

4.7. Antibiolor Internet site: “www.antibiolor.org”
Self-Assessment of Antimicrobial Stewardship in Primary Care: Self-Reported Practice Using the TARGET Primary Care Self-Assessment Tool

Rebecca Owens 1, Leah Ffion Jones 1, Michael Moore 2, Dirk Pilat 3 and Clodna McNulty 1,*

TARGET Self-Assessment Tool

What would be good practice now?

1. Do you use national or local antibiotic guidance when considering how to treat common infections?
   - Yes
   - No

2. Is the latest antibiotic guidance made available to all temporary prescribers working in your surgery?
   - Yes
   - No

3. Do you have a back-up/laid down prescribing when appropriate?
   - Yes
   - No

4. Have you been involved in a practice antibiotic audit in the last two years?
   - Yes
   - No

5. Do you actually record clinical indication for antibiotic prescribed in patient notes using Read Codes?
   - Yes
   - No

6. Reflection notes

What most practices should aim to do soon

7. Is there a GP or nurse prescription within your practice who takes a lead on antibiotic stewardship in the practice?
   - Yes
   - No

8. Do you analyse and discuss antibiotic prescribing at your practice in comparison to local indicators at least once a year?
   - Yes
   - No

9. Do you keep a written record and surgery action plan resulting from antibiotic audits?
   - Yes
   - No

10. Reflection notes

What all antibiotic aware practices should be doing

11. Do you use patient focused strategies to highlight the importance of responsible antibiotic use? For example videos and posters in clinical and waiting areas.
   - Yes
   - No

12. Do you regularly have patient information leaflets around infections within your consultations?
   - Yes
   - No

13. Do you have a strategy to avoid patients re-consulting with other clinicians to obtain antibiotics?
   - Yes
   - No

14. Have you undertaken any antibiotic-related prescribing clinical courses, for example the ‘Managing Acute Respiratory Tract Infection’ and ‘Managing UTI’ training courses on the RCSGP Online Learning Environment?
   - Yes
   - No

15. Reflection notes

Figure 3. A visual breakdown of the five questions from the section entitled “What would be good practice now”.

Figure 5. What all antibiotic aware practices should be doing.
Community pharmacists—Leaders for antibiotic stewardship in respiratory tract infection  


S. Essack BPharm, MPharm, PhD1 |  J. Bell2 |  A. Shephard BSc Hons, CBiol, FSB3

**Table 1** The opportunities community pharmacists have for antibiotic stewardship

<table>
<thead>
<tr>
<th>Antibiotic stewardship for community pharmacists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liaise and consult with prescribers on:</td>
</tr>
<tr>
<td>• Antibiotic prescriptions—to promote adherence to guidelines, appropriate prescribing and optimal treatment regimens</td>
</tr>
<tr>
<td>• Updates to information on antibiotics</td>
</tr>
<tr>
<td>• Ensuring the supply chain of antibiotics meets their needs</td>
</tr>
<tr>
<td>Advise, support and educate patients on:</td>
</tr>
<tr>
<td>• Common ailments—their causes, symptoms and likely duration</td>
</tr>
<tr>
<td>• When they need to see a doctor—following assessment for severity of illness and the identification of any red flags or risk factors for serious infections</td>
</tr>
<tr>
<td>• Symptomatic treatment options for self-limiting illnesses</td>
</tr>
<tr>
<td>• Infection prevention and control—simple hygiene measures, such as handwashing, and education on how infections are caught and transmitted</td>
</tr>
<tr>
<td>• Antibiotics—what they are effective for, what antibiotic resistance is and why it is important</td>
</tr>
<tr>
<td>Promote the appropriate use of prescribed antibiotics, advising patients on:</td>
</tr>
<tr>
<td>• Compliance—the importance of taking the antibiotic as prescribed and following the correct dosage regimen (dose intervals, duration of treatment)</td>
</tr>
<tr>
<td>• Potential adverse effects and what to do if they occur</td>
</tr>
<tr>
<td>• Any risk of interactions</td>
</tr>
<tr>
<td>Disposal of old/unused antibiotics</td>
</tr>
<tr>
<td>Health education and promotion campaigns</td>
</tr>
<tr>
<td>Uphold dispensing regulations and ensure the quality of antibiotics by guarding against counterfeit drugs</td>
</tr>
</tbody>
</table>

![Diagram](image_url)
The Critical Role of the Staff Nurse in Antimicrobial Stewardship—Unrecognized, but Already There

Richard N. Olans,1 Rita D. Olans,2 and Alfred DeMaria Jr.3
1Tuft Health System, Inc., MelroseWakefield Hospital, 2MGH Institute of Health Professions - School of Nursing, Boston, and 3Bureau of Infectious Disease, Massachusetts Department of Health, William A. Nistor State Laboratory Institute, Jamaica Plain, Massachusetts

An essential participant in antimicrobial stewardship who has been unrecognized and underutilized is the "staff nurse." Although the role of staff nurses has not formally been recognized in guidelines for implementing and operating antimicrobial stewardship programs (ASPs) defined in the medical literature, they have always performed numerous functions that are integral to successful antimicrobial stewardship. Nurses are antibiotic first responders, central communicators, coordinators of care, as well as 24-hour monitors of patient status, safety, and response to antibiotic therapy. An operational analysis of inpatient admissions evaluates these nursing stewardship activities and analyzes the potential benefits of nurses’ formal education about, and inclusion into, ASPs.


KEY NURSING ACTIVITIES INCLUDE:

- TRIAGE, AND INITIAL INFECTION CONTROL PRECAUTIONS
- MEDICATION ALLERGY ASSESSMENT AND RECONCILIATION
- TIMELY ORDERING AND ADMINISTRATION OF ANTIBIOTICS

EARLY AND APPROPRIATE COLLECTION AND SUBMISSION OF SPECIMENS FOR CULTURE

- ANTIBIOTIC TIMEOUT AND DE-ESCALATION
- IMPLEMENTATION OF QUALITY AND SAFETY BUNDLE MEASURES

- CENTRAL COMMUNICATOR AMONG PRESCRIBERS, PHARMACY, LAB, DISCHARGE PLANNERS AND CONSULTANTS
Strategies and challenges of antimicrobial stewardship in long-term care facilities

- Unnecessary antibiotic treatments for colonization (e.g., asymptomatic bacteriuria)
- Unnecessary antibiotic treatments for urinary tract infection prophylaxis
- Unnecessary antibiotic treatments for viral infections (e.g., influenza)
- Unnecessary use of topical antibiotics
- Absence of reassessment of antibiotic therapies at around day 3
- Longer-than-necessary durations

<table>
<thead>
<tr>
<th>TABLE 4. Common causes of antibiotic misuse in long-term care facilities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unnecessary antibiotic treatments for colonization</strong> (e.g., asymptomatic bacteriuria)</td>
</tr>
<tr>
<td><strong>Unnecessary antibiotic treatments for urinary tract infection prophylaxis</strong></td>
</tr>
<tr>
<td><strong>Unnecessary antibiotic treatments for viral infections</strong> (e.g., influenza)</td>
</tr>
<tr>
<td><strong>Unnecessary use of topical antibiotics</strong></td>
</tr>
<tr>
<td><strong>Absence of reassessment of antibiotic therapies at around day 3</strong></td>
</tr>
<tr>
<td><strong>Longer-than-necessary durations</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 1. Cross-sectional surveys of antimicrobial stewardship programmes in long-term care facilities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ESAC</strong> [21] Europe <strong>n = 260</strong></td>
</tr>
<tr>
<td>Antimicrobial stewardship committee</td>
</tr>
<tr>
<td>Therapeutic formulary</td>
</tr>
<tr>
<td>Antimicrobial guidelines</td>
</tr>
<tr>
<td>Data about antibiotic consumption</td>
</tr>
<tr>
<td>Data about local antimicrobial resistance profiles</td>
</tr>
<tr>
<td>Regular training of prescribers on antibiotic use</td>
</tr>
<tr>
<td>Individual antimicrobial prescribing profiles</td>
</tr>
<tr>
<td>Pharmacist advice on antibiotic use</td>
</tr>
<tr>
<td>Regular audits assessing antibiotic use</td>
</tr>
<tr>
<td>—, not available.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 2. Main recommended antimicrobial stewardship strategies in long-term care facilities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Discourage antibiotic prescribing without clinical examination</strong></td>
</tr>
<tr>
<td><strong>Education (medical and nursing staff, patients and their families)</strong></td>
</tr>
<tr>
<td><strong>Target areas where antibiotic misuse is common: antibiotic prophylaxis, bacterial colonization, topical antibiotics, durations of treatment (see Table 4)</strong></td>
</tr>
<tr>
<td><strong>Use locally adopted diagnostic and therapeutic guidelines for the most common infections</strong></td>
</tr>
<tr>
<td><strong>Reassess antibiotic treatments at around day 3</strong></td>
</tr>
<tr>
<td><strong>Limit unnecessary microbiological investigations</strong></td>
</tr>
<tr>
<td><strong>Improve the reporting from the microbiology laboratory</strong></td>
</tr>
<tr>
<td><strong>Use point-of-care diagnostic tests</strong></td>
</tr>
<tr>
<td><strong>Test innovative strategies and integrate antimicrobial stewardship programmes in existing quality/safety infection prevention and control programmes</strong></td>
</tr>
</tbody>
</table>
LOTS OF GOOD PRACTICE

NEED TO TAKE A NOVEL SYSTEMS AND HUMAN FACTORS APPROACH TO IMPLEMENTING STEWARDSHIP
From: Implementing Antimicrobial Stewardship in Long-term Care Settings: An Integrative Review Using a Human Factors Approach
Clin Infect Dis | © The Author 2017. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com.
AMS in human is a whole systems approach: doing AMS in isolation in one component of the system will not be successful in the long term.
Lessons learnt during 20 years of the Swedish strategic programme against antibiotic resistance

Sigvard Mölstad, Sonja Löfmark, Karin Carlin, Mats Erntell, Olov Aspevall, Lars Biao, Hakan Hanberger, Katarina Hedén, Jenny Hellman, Christer Norman, Gunilla Skoog, Cecilia Stålsby-Lundborg, Karin Tegmark Wisell, Christina Åhrén & Otto Cars

Box 3. Systems and tools in Sweden to monitor prescribers’ adherence to antibiotic treatment recommendations

• Point prevalence surveys of infections1,2 and antibiotic use in primary health care (years 2000, 2002, and 2005). Manual registrations were made by general practitioners in 571 counties, covering the doctor’s diagnosis, the use of diagnostic tests, symptoms and signs and antibiotic treatment during one week each year.
• System for receiving data on antibiotic prescribing and diagnosis collected annually (since year 2000) from the primary health-care register of infections in Sweden. Data are extracted from medical records from 60-90 primary health-care centres, with a listed population of approximately 500,000 inhabitants out of the total population of 10 million.
• Project to develop standardized collection and evaluation of data from electronic medical records in primary health care that is uniform and comparable over time (started at the Public Health Agency of Sweden in the year 2013).13
• Annual national point prevalence survey on antibiotic consumption and health care-associated infections in long-term care facilities (started at the Public Health Agency in the year 2014),14 with the aim of supporting preventive work.
• Point prevalence surveys of infections and antibiotic use in a large sample of Swedish acute care hospitals by local multiprofessional groups (years 2003, 2004, 2005, 2006 and 2010).11,13
• Point prevalence surveys of health-care associated infections performed by health-care providers and the Swedish Association of Local Authorities and Regions (twice yearly 2008 to 2014 and then annually).
• System for extracting data on the indications for antibiotic treatment, diagnoses and risk factors, and on operations and other patient interventions. Data are extract from electronic health records at the point of prescription. The antibiotic tool was launched in 2010 by the Swedish Association of Local Authorities and Regions and was implemented in nearly all Swedish hospitals by 2014. Local multiprofessional groups have an important role in the interpretation and feedback of data to prescribers.
STRUCTURAL INDICATORS

Measure whether governance structures are in place for stewardship such as: Does a hospital have an antimicrobial team which meets regularly, reports to senior management and has an action plan?

PROCESS INDICATORS

Measure systems in place for stewardship such as a surveillance programme for antibiotic use, a programme of audits, education for healthcare staff.

OUTCOME INDICATORS

Are used to measure the impact of a stewardship programme and should include both intended and unintended outcomes such as reduced use of restricted antibiotics (intended) and increase in resistance to recommended antibiotics (unintended).
### Table 3. The final set of 12 evidence-based and consensually validated quantity metrics for antibiotic use in the inpatient setting

<table>
<thead>
<tr>
<th>Inpatient quantity metric (IQM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IQM 1: Defined daily doses (DDDs) per 100(0) PDs/BDs/OBDs&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>IQM 2: Defined daily doses (DDDs) per admission</td>
</tr>
<tr>
<td>IQM 3: Defined daily doses (DDDs) per (100 bed-days per CMI)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>IQM 4: Prescribed daily doses (PDDs) per 100 PDs</td>
</tr>
<tr>
<td>IQM 5: Days of therapy (DOT) per PD</td>
</tr>
<tr>
<td>IQM 6: Days of therapy (DOT) per patient</td>
</tr>
<tr>
<td>IQM 7: Days of therapy (DOT) per admission</td>
</tr>
<tr>
<td>IQM 8: Length of therapy (LOT) per admission</td>
</tr>
<tr>
<td>IQM 9: Length of therapy (LOT) per patient</td>
</tr>
<tr>
<td>IQM 10: Patients exposed to antibiotics per all patients</td>
</tr>
<tr>
<td>IQM 11: Patients exposed to antibiotics per admission</td>
</tr>
<tr>
<td>IQM 12: Antibiotic use should be preferably expressed in at least two metrics simultaneously</td>
</tr>
</tbody>
</table>

<sup>a</sup>100(0) patient-days (PD)/bed-days (BDs)/occupied bed-days (OBDs).  
<sup>b</sup>CMI, case mix index. This is a relative value assigned to a diagnosis-related group of patients in a medical care environment.
A systematic review of quality indicators for appropriate antibiotic use in hospitalized adult patients

Marlot C. Kallen, Jan M. Prins
Department of Internal Medicine, Division of Infectious Diseases, Academic Medical Centre, University of Amsterdam, the Netherlands

Table 2. Description of the top 10 retrieved quality indicators.

<table>
<thead>
<tr>
<th>Developed Indicators</th>
<th>Number of articles mentioning the indicator/total number of articles</th>
<th>Percentage of articles mentioning the indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescribe empirical antibiotic therapy according to (local or national) guidelines</td>
<td>10/14</td>
<td>71</td>
</tr>
<tr>
<td>Switch from intravenous to oral therapy</td>
<td>9/14</td>
<td>64</td>
</tr>
<tr>
<td>Perform at least two sets of blood cultures</td>
<td>8/14</td>
<td>57</td>
</tr>
<tr>
<td>Change to pathogen-directed therapy when culture results become available</td>
<td>8/14</td>
<td>57</td>
</tr>
<tr>
<td>Timely initiation of antibiotic therapy</td>
<td>7/14</td>
<td>50</td>
</tr>
<tr>
<td>Adapt dose and dosing interval of antibiotics to renal function</td>
<td>7/14</td>
<td>50</td>
</tr>
<tr>
<td>Documentation of antibiotic plan in medical record</td>
<td>7/14</td>
<td>50</td>
</tr>
<tr>
<td>Perform a site culture</td>
<td>6/14</td>
<td>43</td>
</tr>
<tr>
<td>Discontinue antibiotic therapy if infection not confirmed</td>
<td>6/14</td>
<td>43</td>
</tr>
<tr>
<td>Duration of antibiotic therapy</td>
<td>6/14</td>
<td>43</td>
</tr>
</tbody>
</table>
Antimicrobial consumption and resistance in adult hospital inpatients in 53 countries: results of an internet-based global point prevalence survey

Ann Versporten, Peter Zarb, Isabelle Caniaux, Marie-Françoise Gros, Nico Drapier, Mark Miller, Vincent Jarlier, Dilip Nathwani, Herman Goossens, on behalf of the Global-PPS network*

| Region                          | Antimicrobial prescriptions | Antibiotic prescriptions | Targeted treatment* | Targeted treatment (resistant organisms)* | Reason recorded† | Stop or review date recorded† | Parenteral administration‡ | Guidelines available§ | Compliant to local guidelines¶ | No guidelines available||
|---------------------------------|-----------------------------|--------------------------|---------------------|-------------------------------------------|------------------|--------------------------------|--------------------------|------------------------|---------------------------------|-----------------------------|
| Eastern Europe (n=653)          | 747                         | 708                      | 51 (7.8%)           | 42 (6.4%)                                 | 64.3%            | 50.5%                          | 87.6%                    | 79.8%                  | 85.7%                           | 19.2%                       |
| Northern Europe (n=2783)        | 3880                        | 3536                     | 396 (14.2%)         | 80 (2.9%)                                 | 81.4%            | 51.6%                          | 62.2%                    | 90.0%                  | 83.4%                           | 6.5%                        |
| Southern Europe (n=5534)        | 7674                        | 6837                     | 838 (15.1%)         | 292 (5.3%)                                | 69.5%            | 29.1%                          | 80.0%                    | 60.5%                  | 70.8%                           | 29.6%                       |
| Western Europe (n=8458)         | 10612                       | 9485                     | 2204 (26.1%)        | 469 (5.5%)                                | 80.5%            | 40.3%                          | 64.0%                    | 81.0%                  | 78.7%                           | 10.1%                       |
| Africa (n=899)                  | 1502                        | 1213                     | 131 (14.6%)         | 25 (2.8%)                                 | 70.4%            | 43.5%                          | 71.8%                    | 76.4%                  | 81.5%                           | 21.4%                       |
| East and south Asia** (n=5363)  | 7607                        | 6781                     | 938 (17.5%)         | 287 (5.4%)                                | 74.6%            | 43.5%                          | 71.8%                    | 76.4%                  | 81.5%                           | 21.4%                       |
| West and central Asia (n=1612)  | 2252                        | 2084                     | 236 (14.6%)         | 153 (9.5%)                                | 72.8%            | 19.8%                          | 85.2%                    | 53.4%                  | 66.3%                           | 40.5%                       |
| Oceania (n=932)                 | 1411                        | 1226                     | 218 (23.4%)         | 63 (6.8%)                                 | 85.1%            | 27.0%                          | 60.5%                    | 87.4%                  | 73.2%                           | 11.7%                       |
| Latin America (n=1518)          | 2403                        | 2170                     | 403 (26.5%)         | 231 (15.2%)                                | 81.4%            | 40.3%                          | 84.4%                    | 76.5%                  | 64.1%                           | 19.9%                       |
| North America (n=2139)          | 3125                        | 2752                     | 511 (23.9%)         | 127 (5.9%)                                | 84.9%            | 39.6%                          | 73.1%                    | 77.3%                  | 85.8%                           | 18.5%                       |
| Total (n=29891)                 | 41213                       | 36792                    | 5926 (19.8%)        | 1769 (5.9%)                                | 76.9%            | 38.3%                          | 71.4%                    | 74.3%                  | 77.4%                           | 19.2%                       |

Data are n or %. A version of this table containing numerical data for all percentages is in the appendix. *Patients receiving at least one antibiotic for systemic therapeutic use only (ie, health-care-associated or community-acquired infection). †Includes all antimicrobials; the total number of antimicrobial prescriptions was used to calculate percentages. ‡Patients who received at least one parenteral antibiotic for systemic use. §Antibiotic prescriptions for which guidelines were available to guide antibiotic choice (not route, dose, or duration), which was calculated as all antibiotic prescription for which a local guideline was available/all antibiotic prescription. ¶The number of antibiotic prescriptions for which guidelines were available was used as the denominator to calculate percentages. **Includes south, east, and southeast Asia.

Table 4: Overview of antimicrobial and antibiotic quality indicators for adult inpatients by region, year 2015
ANTIBIOTIC PRESCRIBING INDICATORS/METRICS

**Process measures**
- Promoted antibiotic
- Restricted antibiotics
- Days or length of therapy
- 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”

**Outcome measures**
- Antibiotic consumption rates
- CDI rates
- SSI rates
- Surveillance of resistant pathogens
- Mortality [SMR’s]
- Cost of pharmaceuticals
- LOS

**Balancing measures**
- 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
A framework for ensuring a balanced accounting of the impact of antimicrobial stewardship interventions

Madalina Toma¹, Peter G. Davey², Charis A. Marwick² and Bruce Guthrie¹,²,*

Definitely expected from outset
Define goals and trade-offs;
Develop initial measurement plan;
Consider costs

Definitely unexpected from outset
Improvement pause to define surprises;
Develop new measurement strategy;
Consider costs

Expectation spectrum

Desirable
Antimicrobial stewardship intervention
Predefined Goals

Undesirable
Antimicrobial stewardship intervention
Predefined trade-offs

All four consequences can be measured using either process or outcome measures
All four consequences can arise in the same area of care targeted by the antimicrobial stewardship intervention or elsewhere in the health and social care system

J Antimicrob Chemother 2017; 72: 3223–3231

The law of unintended consequences is the only real law of history.
—Niall Ferguson—
Effect of a national 4C antibiotic stewardship intervention on the clinical and molecular epidemiology of Clostridium difficile infections in a region of Scotland: a non-linear time-series analysis

Timothy Lawes, José-Maria Lopez-Lozano, Cesar A Nebot, Gillian Macartney, Rashmi Subbarao-Sharma, Karen D Wares, Carolyn Sinclair, Ian M Gould

Desirable outcome:
A framework for ensuring a balanced accounting of the impact of antimicrobial stewardship interventions

Madalina Toma¹, Peter G. Davey², Charis A. Marwick² and Bruce Guthrie¹,²,*

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Predefined Goals

Undesirable
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Predefined trade-offs

Antimicrobial stewardship intervention
Pleasant surprises

Antimicrobial stewardship intervention
Unpleasant surprises

All four consequences can be measured using either process or outcome measures
All four consequences can arise in the same area of care targeted by the antimicrobial stewardship intervention or elsewhere in the health and social care system

J Antimicrob Chemother 2017; 72: 3223–3231
### CQUIN 2017/19

<table>
<thead>
<tr>
<th>Aim</th>
<th>Deliverable</th>
</tr>
</thead>
</table>
| Improve detection and treatment of sepsis| - Timely identification of sepsis in EDs and acute inpatient settings  
- Timely treatment (% of patients with sepsis who received IV antibiotics within 1 hour)  
- Antibiotic review within 24-72 hours |
| Improve antibiotic prescribing           | - Reduction in antibiotic consumption per 1,000 admissions  
- Total antibiotic usage  
- Carbapenem usage  
- Pip/tazobactam usage |

### Quality Premium 2017/19

<table>
<thead>
<tr>
<th>Aim</th>
<th>Deliverable</th>
</tr>
</thead>
</table>
| Improve antibiotic prescribing           | - Sustained reduction of inappropriate antibiotic prescribing in primary care  
- Items/STAR-PU equal to or below England 2013/14 mean value  
- Reduction of inappropriate antibiotic prescribing in UTI in primary care  
- 10% reduction in Trimethoprim/Nitrofurantoin prescribing ratio  
- 10% reduction in trimethoprim items for patients aged 70 years or more |
| Reduce Gram-ve BSIs across whole health economy | - Reduction of 10% in all *E. coli* BSI reported at CCG level independent of time of onset  
- Collect and report a core primary care data set for all *E. coli* BSI in Q2-4 2017/18 |
DOES MORE TIMELY TREATMENT WITH ANTIBIOTICS OFFERS REDUCED MORTALITY IN SEPSIS & SEPTIC SHOCK?

- N = ~85000, hospitalized, US retrospective data base [1,2]
- Only beneficial difference in mortality in patients with septic shock

- N=2018, pre-hospital v EM, Netherlands, >95% of patients no septic shock [3]
- 96 mins median earlier time to administration of antibiotics

- **No difference is mortality** in those without septic shock

- **Antibiotic may being used without care and causing harm**
**Sepsis** is medicine's last remaining preserve for unrestrained antibiotic prescribing. The Surviving Sepsis Campaign guidelines recommend empirical broad-spectrum therapy within one hour of triage for both sepsis and septic shock.¹ This recommendation, and mandates that compel it, encourage clinicians to adopt an approach of "treat first, ask questions later" for patients with any possibility of serious infection. This approach fails to account for the difficulties clinicians face with diagnosing infection, especially when patients initially present to care, and the high rate of overdiagnosis of sepsis, and thus risks promoting excess antibiotic use and causing unintended harm.

**Antibiotics for Sepsis—Finding the Equilibrium**

The time has come to balance the recommendation for early and aggressive antibiotics for all patients with possible sepsis with the diagnostic uncertainty regarding sepsis and the possible harm associated with unnecessary antibiotics.
Table 1. Candidate measurements to be considered as part of monitoring AMR and its control.

<table>
<thead>
<tr>
<th>Component</th>
<th>DPSR framework</th>
<th>Measurements</th>
<th>Rationale</th>
<th>Data source and feasibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Process: drivers, knowledge, norms, and behavior</td>
<td>Drug forces: determine the human need for antibiotics</td>
<td>Burden of infectious diseases in human and animal health</td>
<td>The burden of infectious diseases drives the use of antibiotics in the first place</td>
<td>Data on infectious disease burden are compiled by WHO and HME</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Access to sanitation, safe drinking water, and waste water treatment</td>
<td></td>
<td>Data on the status of sanitation facilities are available from WHO/UNICEF</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consumption of meat products</td>
<td>Intensive farming drives antibiotic use in agriculture</td>
<td>Data compiled by FAO</td>
</tr>
<tr>
<td></td>
<td>Pressure: Both quantity and quality of antibiotic use exert pressure (over- and misuse of antibiotics)</td>
<td>Overall consumption of antibiotics in human and animal health</td>
<td>Estimate of selection pressure behind the correlation between use and resistance</td>
<td>Global estimates in the literature (22,23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nonprescription availability (over the counter)</td>
<td>Nonprescription availability and misuse (proxy for strength of the regulatory framework)</td>
<td>Can be measured through testing (systematic review conducted in 2011) (24)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Awareness of AMR among public and health professionals</td>
<td>Lack of awareness drives misuse of antibiotics</td>
<td>Various data from literature; WHO multicountry study in 2015</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Access to quality antimicrobials in hospitals and community</td>
<td>Access to quality antimicrobials reduces misuse in human health</td>
<td>The proportion of the population with access to affordable, essential drugs on a sustainable basis is computed by the UN</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Appropriate use of antibiotics in hospitals and community</td>
<td>Inappropriate use of antibiotics is a driver of resistance. Adherence to best practices in terms of use can reduce the overall consumption of antibiotics</td>
<td>Some data in the literature (US CDC and ECDC)</td>
</tr>
<tr>
<td>Outcomes: current situation and burden of AMR</td>
<td>State: AMR epidemiology</td>
<td>Prevalence of most important resistant pathogens in hospitals, the community, and agriculture</td>
<td>Measure of the magnitude of the problem</td>
<td>Various data are collected at the national and regional level; WHO report on surveillance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Impact on human health and societies</td>
<td>Human health burden of AMR from important pathogens for public health (morbidity and mortality)</td>
<td>Estimates from literature and national centers for disease control</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Economic burden of AMR</td>
<td>Current impact of AMR as an economic cost for society</td>
<td>Estimates from literature</td>
</tr>
<tr>
<td>Structure: policy and regulatory strategy framework</td>
<td>Responses in management tactics</td>
<td>Adoption of a national action plan based on the WHO global action plan</td>
<td>Measure of countries’ basic commitment to tackle AMR</td>
<td>Up-to-date database available from WHO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Implementation of infection prevention and control</td>
<td>Infection prevention and control reduces spread of AMR pathogens, long the AMR reservoir, and curbs antibiotic use</td>
<td>WHO country situation analysis (25) and data available in the literature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Regulation of agriculture to limit nontherapeutic use of antibiotics</td>
<td>Agricultural use drives resistance via the physical environment and food chain</td>
<td>WHO country situation analysis; policy and regulation data in literature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Regulation of antibiotic use in human and nonhuman use</td>
<td>When antibiotics are effectively regulated, it contributes to reduced misuse</td>
<td>WHO country situation analysis; data in the literature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Existence of surveillance programs for AMR and antimicrobial use</td>
<td>Surveillance is a key component to adapt guidelines and guide action on AMR</td>
<td>WHO country situation analysis; data in the literature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antibiotic stewardship programs in hospitals and communities</td>
<td>Antibiotic stewardship improves the appropriate use of antibiotics</td>
<td>Few data from literature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>National public awareness campaign</td>
<td>Informed citizens are more likely to use resources wisely</td>
<td>Estimates from literature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Regulation of antibiotic promotion</td>
<td>Promotional practices can drive overuse</td>
<td>Various data in literature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Financial support for the development of new technologies</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


https://doi.org/10.1371/journal.pmed.1002378.1001
Box 1.
Sample joint vision statement for fighting AMR

We, the health care workers, accept the responsibility to improve patient care and health outcomes by protecting against the emergence and spread of antimicrobial resistance for patients and society, now and in the future. We shall achieve this goal by acquiring and maintaining the competencies related to AMR control including through improving leadership, awareness, knowledge, skills, attitudes and behavioural change regarding the appropriate prescription, dispensing and use of antimicrobials, and implementing better infection prevention and control and diagnostic stewardship.

WHO COMPETENCY FRAMEWORK
FOR HEALTH WORKERS’ EDUCATION
AND TRAINING ON ANTIMICROBIAL RESISTANCE

The framework is configured in a tabular matrix format, containing core and additional AMR competencies, which have been organized across four domain areas and four categories of health workers. The domain areas include: foundations that build awareness of antimicrobial resistance, appropriate use of antimicrobial agents, infection prevention and control (IPC), and diagnostic stewardship and surveillance. The four categories of health worker groupings identify competencies that are required for: all health workers, prescribers, non-prescribers and public health officers/health services managers. This framework provides users with a reference tool to guide the analysis, framing and adaptation of locally relevant education and training materials on AMR.
2 key messages: Achieving stewardship and implementation outcomes.

Structure [S] + Process [P] (+ implementation [i]) + culture = outcomes

VA Antimicrobial Stewardship Initiative

Antimicrobial stewardship interventions
- Intravenous to oral conversation tool
- Avoidance of double anaerobic coverage
- Intervention to improve outcomes for patients with CDI
- Stewardship monitoring of outpatient parenteral antibiotic therapy
- Vancomycin de-escalation

Implementation strategies
- Conduct educational meetings
- Develop educational materials
- Conduct ongoing training
- Distribute educational materials
- Create new clinical teams

Implementation outcomes
- Acceptability
- Appropriateness
- Adoption
- Costs
- Feasibility
- Fidelity
- Penetration
- Sustainability

Antimicrobial stewardship outcomes
- Antimicrobial appropriateness
- Antimicrobial usage
- Antimicrobial resistance
- Clostridium difficile
- Re-admissions

Chaudoir, Dugan, Barr, IS, 2013, 8:22; Kelly et al, ICHE, 2017

THANK YOU