A global call from five countries to collaborate in antibiotic stewardship: united we succeed, divided we might fail

Debra A Goff, Ravina Kullar, Ellie J C Goldstein, Mark Gilchrist, Dilip Nathwani, Allen C Cheng, Kelly A Cairns, Kevin Escandón-Vargas, Maria Virginia Villegas, Adrian Brink, Dena van den Bergh, Marc Mendelson

In February, 2016, WHO released a report for the development of national action plans to address the threat of antibiotic resistance, the catastrophic consequences of inaction, and the need for antibiotic stewardship. Antibiotic stewardship combined with infection prevention comprises a collaborative, multidisciplinary approach to optimise use of antibiotics. Efforts to mitigate overuse will be unsustainable without learning and coordinating activities globally. In this Personal View, we provide examples of international collaborations to address optimal prescribing, focusing on five countries that have developed different approaches to antibiotic stewardship—the USA, South Africa, Colombia, Australia, and the UK. Although each country’s approach differed, when nurtured, individual efforts can positively affect local and national antimicrobial stewardship programmes. Government advocacy, national guidelines, collaborative research, online training programmes, mentoring programmes, and social media in stewardship all played a role. Personal relationships and willingness to learn from each other’s successes and failures continues to foster collaboration. We recommend that antibiotic stewardship models need to evolve from infection specialist-based teams to develop and use cadres of health-care professionals, including pharmacists, nurses, and community health workers, to meet the needs of the global population. We also recommend that all health-care providers who prescribe antibiotics take ownership and understand the societal burden of suboptimal antibiotic use, providing examples of how countries can learn, act globally, and share best antibiotic stewardship practices.

Introduction
Antimicrobial resistance represents arguably the greatest current public health threat. If the increase in drug resistance is not slowed, modelling suggests that from the current 700,000 deaths annually, deaths attributed to drug-resistant infections by 2050 will surpass 10 million—ie, one person dying every 3 s.¹ The cost to global economic output is estimated at US$100 trillion. Overuse of antibiotics, the main driver of resistance, pervades all of society. High levels of animal protein production through intensive farming have long been supported by the use of subtherapeutic concentrations of antibiotics to promote growth and reduce the time to market, and by wide-scale treatment (metaphylaxis) of healthy fed animals with antibiotics to prevent infections. The intense selection pressure this method of farming confers has selected out multidrug-resistant bacteria in animals that have found their way into the human population.²³ Misuse of antibiotics for treatment of viruses causing upper respiratory tract infections and acute bronchitis in the community, and inappropriate use in hospitals have resulted in selection of so-called superbugs—multidrug-resistant bacteria that are either sensitive to only last resort antibiotics or those that are panresistant.⁴

Entry into a post-antibiotic era constitutes a global threat, which requires an international collaborative response. The Lancet Infection Diseases Commission⁵ and WHO⁶ have highlighted the need for a collaborative approach to support resource-limited countries in optimising antibiotic use through education and stewardship, and the need for the development of action plans. Antibiotic stewardship programmes can decrease antibiotic use while maintaining or improving antibiotic resistance.⁷ In this Personal View, we describe antimicrobial stewardship from five countries, two of which are resource-limited, that have collaborated through research, education, and outreach to affect global antibiotic resistance.

Antimicrobial stewardship in the USA
History and implementation process
Antibiotic stewardship was first formalised as a programmatic activity in 2007 by both the Infectious Diseases Society of America and Society for Healthcare Epidemiology of America. They described antibiotic stewardship as “a multidisciplinary approach by a team consisting of infectious disease clinicians, pharmacists, microbiologists, hospital epidemiologists, and infection preventionists”.⁸ Core strategies (perspective audit and feedback, and formulary restriction and preauthorisation) and supplemental elements (education, guidelines and clinical pathways, antimicrobial order forms, streamlining or de-escalation, dose optimisation, and parental to oral conversion) were recommended. A 2016 update provided a more practical approach for sustainability, recommending antimicrobial stewardship programmes to implement rapid diagnostics, syndrome-specific interventions, and customising interventions on the basis of local issues, resources, and expertise.⁹ Despite this update, antibiotic resistance has continued to increase.¹⁰ California is the only state to mandate stewardship,¹⁰ although others have implemented programmes with substantial effect on patient outcomes.¹¹,¹² Sadly, only 39% of US hospitals in 2014 had antimicrobial stewardship programmes.¹³,¹⁴ By 2017, all US facilities will be required to develop and implement them.¹⁵ President Barack Obama’s national action plan¹⁶ for combating antimicrobial-resistant

Lancet Infect Dis 2016
Published Online
November 17, 2016
http://dx.doi.org/10.1016/S1473-3099(16)30386-3
The Ohio State University College of Pharmacy, The Ohio State University Wexner Medical Center, Columbus, OH, USA (D A Goff PharmD); Merck Research Laboratories, Merck & Co, Kenilworth, NJ, USA (R Kullar PharmD); R M Alden Research Laboratory, Los Angeles, CA, USA (Prof E J C Goldstein MD); UCLA School of Medicine, University of California, Los Angeles, CA, USA (Prof E J C Goldstein); Department of Infection and Pharmacy, Imperial College Healthcare NHS Trust, Charing Cross Hospital, London, UK (M Gilchrist MPharm); Infection Unit, Ninewells Hospital and Medical School, Dundee, UK (D Nathwani MB); School of Medicine, Monash University, Clayton, VIC, Australia (Prof A C Cheng PhD); Infection Prevention and Healthcare Epidemiology Unit (Prof A C Cheng) and Pharmacy Department (K A Cairns BPharm), Alfred Health, Melbourne, VIC Australia; Bacterial Resistance and Hospital Epidemiology Area, International Center for Medical Research and Training (CIDEIM), Cali, Colombia (K Escandón-Vargas MD, M V Villegas MD); Ampath National Laboratory Services, Milpark Hospital, Johannesburg, South Africa; Alfred Health Melbourne, VIC Australia; Bacterial Resistance and Hospital Epidemiology Unit, International Center for Medical Research and Training (CIDEIM), Cali, Colombia (K Escandón-Vargas MD, M V Villegas MD); or any corresponding author.
bacteria has doubled federal funding for antibiotic resistance research in 2016. It recommended that centres for Medicare and Medicaid services monitor antibiotic use and resistance, through the National Healthcare Safety Network Antimicrobial Use and Resistance module.

Education and support
The Infectious Diseases Society of America provides treatment guidelines for specific infections. Several free, online stewardship toolkits have been developed, such as from Stanford University, which offers three massive open-ended online courses (including Continuing Medical Education) on various stewardship topics (table). These courses include “Antimicrobial stewardship: optimisation of antibiotic practices” (as of May, 2016, 37470 people had enrolled from >120 countries), “Optimising antibiotics with timeouts” (as of August, 2016, 1071 people had enrolled), and “To prescribe or not to prescribe? Antibiotics and outpatient infections” (which will be promoted by the US Centers for Disease Control and Prevention for a release date of November, 2016). The Infectious Diseases Association of California has held antibiotic stewardship training courses since 2011, with more than 1000 people attending. Making a Difference in Infectious Diseases and The Society of Infectious Diseases Pharmacists offer stewardship certification programmes. Further, the American Society of Health-System Pharmacists provides onsite mentoring to help hospitals to implement or enhance their programmes. Unique to the USA, clinical pharmacists can specialise in infectious diseases through a residency of infectious diseases accredited by the American Society of Health-System Pharmacists.

Lastly, collaborative Twitter platform-based grand rounds between the US, European, and Australian partners engage health-care providers and increase public awareness of antibiotic resistance. Twitter provides a way for stewards to connect, engage, educate, and share antibiotic research.

Future directions
The Joint Commission’s new antimicrobial stewardship standards will be effective in January, 2017, and will be required by all US hospitals. Key components include use of electronic health records to collect data, education to clinicians upon hire or granting of initial prescribing privileges and periodically thereafter, education to patients and their families, implementation of hospital approved multidisciplinary protocols, and assessment of ongoing treatment need (ie, antibiotic timeout after 48 h). Although electronic health records and clinical decision support systems have benefitted clinicians in daily stewardship duties, better integration of outcome metrics are needed within these systems. Each hospital is expected to take action on improvement opportunities identified in its antimicrobial stewardship programme through the use of rapid diagnostics, which reduce treatment delay. Commitment is needed for further development, for appropriate use, and to extend stewardship to microbiology. The US Centers for Disease Control and Prevention has also developed an antibiotic use option that collects and reports monthly antibiotic use data. This benchmarking of data has been identified as a high priority for the USA.

Antimicrobial stewardship in South Africa
History and implementation process
For more than two decades, HIV and tuberculosis have dominated South Africa’s health system, offering little space for the growing burden of antibiotic resistance until the antiretroviral therapy programme was rolled out. Inadequate trained personnel, education, and public awareness have compounded the problem.

South Africa’s antibiotic resistance strategy success is attributed to strong leadership from the Minister and
Director General of Health, in partnership with the South African Antibiotic Stewardship Programme as a technical advisor. The programme spans public and private, human, and animal sectors—providing leadership, advocacy for, and strengthening of antibiotic resistance interventions—and the programme is in a partnership with the national government to develop the national strategy framework and implementation policy.

National governance is provided by a ministerial advisory committee, comprising intersectoral stakeholders, and is involved in coordinating efforts (including antibiotic resistance monitoring) and assessing implementation. National core standards, overseen by an Office for Health Standards Compliance, are mandatory for all health institutions and ensure accountability.

South Africa’s strategy draws on their strengths in national structured surveillance and reporting systems on antibiotic use to inform selection of antibiotics for the South African essential drugs programme. In partnership with the Centre for Disease Dynamics, Economics, and Policy, resistance maps that show provincial variation in overall use of antibiotics allow prioritisation of interventions.

Several antimicrobial stewardship programme models have been reported. In a single-centre study, combined stewardship ward rounds with a dedicated antibiotic prescription chart showed a roughly 20% reduction in antibiotic use without harm. A non-specialised pharmacist-led study showed a similar reduction in overall use of antibiotics. A pharmacist-driven prospective audit and feedback study of eight process and outcome measures, relating to compliance with the South African community-acquired pneumonia guidelines in public and private hospitals, is underway.

**Future directions**

Uniform adoption of antibiotic resistance and infection prevention best practices across South Africa’s nine provinces is directed by the national government. Education programmes for health-care provider groups will run at regional training centres. Core curricula for health and veterinary students, and for school learners are in development. Public awareness campaigns using four of the national health awareness days are also in development.

**Antimicrobial stewardship in Colombia**

**History and implementation process**

Although Colombia is a resource-limited country, a promising opportunity for stewardship has occurred in the past years. In 2001, the International Centre for Medical Research and Training (CIDETM) developed the Colombian Nosocomial Resistance Study Group, a network comprising 31 public and private hospitals in 12 cities, to track antibiotic resistance based on half yearly data submitted by the hospitals to the centre.

---

### Table: Antimicrobial stewardship education tools to assist health-care providers

<table>
<thead>
<tr>
<th>Type of education tool</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic Guardian: a call to action to make better use of antibiotics</td>
<td>Campaign <a href="http://www.antibioticguardian.com">www.antibioticguardian.com</a></td>
</tr>
<tr>
<td>Driving Reinvestment in Research and Development and Responsible Antibiotic Use</td>
<td>Project <a href="http://drive-ab.eu/">http://drive-ab.eu/</a></td>
</tr>
</tbody>
</table>
Antimicrobial stewardship in Australia

History and implementation process

Stewardship in Australia has gradually evolved from antimicrobial stewardship programmes led by hospital-based infectious disease physicians and clinical microbiologists to encompass the full breadth of the health-care system. Early examples of coordination include the establishment of voluntary hospital-based surveillance programmes and standardised national treatment guidelines (table). Since 2001, hospital-based clinical decision support systems have been developed by infectious disease physicians and pharmacists to support stewardship.46

Education and support

In recognition of the negative effect of use of antibiotics in food-producing animals,47 the Expert Advisory Group on Antibiotic Resistance developed a risk assessment approach of antibiotic classes to human health, which resulted in a successfully coordinated public policy to protect key antibiotics. For instance, the use of fluoroquinolones has been heavily restricted—at a clinical level to second-line indications in clinical practice guidelines, at a financial level by the restriction of reimbursable indications by the national Pharmaceutical Benefits Scheme, and at a regulatory level by a moratorium on licensure in food-producing animals.43

Increasing government awareness of antibiotic stewardship was catalysed by the 2011 National Antimicrobial Resistance Summit—coordinated by the Australasian Society for Infectious Diseases and the Australian Society for Antimicrobials—to highlight the growing threat of antibiotic resistance and need for a co-ordinated national response. The subsequent formation of the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance has consolidated existing fragmented systems. Substantial contributions from government agencies have provided a state of the nation report, including an overview of antibiotic use in primary care settings,45 veterinary medicine, and food production industries,46 as well as a summary of surveillance systems.47

Since 2007, a substantial expansion of antimicrobial stewardship programmes and national surveillance activities has occurred. Widespread implementation of national guidelines for stewardship47 and its adoption, has been driven by stewardship’s inclusion in the National Safety and Quality Health Service Standards required for hospital accreditation.47 Surveillance of volume-based antibiotic use has expanded since 2004, from 15 to more than 150 hospitals nationally, supported by the Australian Commission for Safety and Quality in Health care that has facilitated national and international benchmarking of antimicrobial use.48 The National Centre for Antimicrobial Stewardship coordinates quality-based surveillance through the National Antimicrobial Prescribing Survey, which was done by 151 hospitals in 2013.47

References

40 Generics antibiotics, which are associated with higher mortality rates compared with brand name antibiotics.40 Research has also influenced stewardship strategies in the assessment of generic antibiotics, which are associated with higher mortality rates compared with brand name antibiotics.40 Generics in Colombia are not bioequivalent to the branded product.40 Access to assured quality antibiotics is an important factor in Colombia’s antimicrobial stewardship programmes. Surveillance of resistance helps to guide interventions, and regional surveillance efforts have increased in the Americas. A novel electronic tool installed on a mobile tablet collects real-time, standardised health-care-associated infections and antibiotic use data for hospitals. An individual improvement plan was suggested for each hospital after assessment of its implementation.38

Future directions

Experience in Colombia has shown the value of a multidisciplinary approach, including physicians, microbiologists, and infection preventionists; however, as in other Latin American countries, pharmacists can dispense medications but do not participate in ward rounds or have an active role in stewardship. Collaboration with US partners to participate in mentoring programmes is a future goal. Further, establishing nationwide policies supporting health-care providers dedicated full time to stewardship and infection prevention committee development are underway.38,40
In 2015, the Australian Government released Australia’s first antibiotic resistance strategy (table). Elements include the need to raise awareness on appropriate antibiotic usage and to implement stewardship tailored to a variety of settings, development of surveillance across human and animal health, the role of infection prevention, the need for research to promote new approaches and products, and the need to strengthen national and international governance.

Future directions
Additional work is required to implement the national strategy, while retaining the strong clinician engagement that has been a feature of stewardship in Australia. Progress is being made towards a coordinated surveillance system through the Antimicrobial Use and Resistance in Australia Project. The government-funded National Prescribing Service started a so-called resistance fighter campaign to train and educate primary care providers and the public. Coordination of similar resources is needed for hospital-based prescribers and clinical pharmacists, because resources differ markedly between different states and territories. Additionally, there has been a poor uptake of electronic prescribing in Australian hospitals, which limits the scope of surveillance; however, a national electronic health record is planned.

Antimicrobial stewardship in the UK
History and implementation process
Antimicrobial stewardship within the UK gained momentum in the early 2000s because of an increase in antibiotic resistance, *Clostridium difficile* infection, and the recognition that antibiotic overprescribing was occurring. These issues were initially addressed by a 3-year Department of Health initiative that provided £12 million of funding to hospital pharmacies, allowing hospitals to update anti-infective guidelines, initiate joint ward rounds, implement surveillance and audits, and increase education. This funding helped to reduce meticillin-resistant *Staphylococcus aureus* bacteraemia and *C difficile* infection. In Scotland, the Government funded the Scottish Antimicrobial Prescribing Group, which successfully reduced rates of *C difficile* infection, stabilised antibiotic resistance, and introduced national and local prescribing metrics with feedback to mandate appropriate antibiotic use. In 2016, national antibiotic toolkits and guidance around the antibiotic practice, systems, and processes were introduced (table).  

Education and support
The first national antibiotic prescribing and stewardship competencies were published in 2013, which discussed the activity and outcomes that prescribers should be able to show. Although not strictly enforced, competencies are used as a framework to enable local stewardship teams to promote best practice. In 2014, to help raise awareness and engagement of resistance, the Antibiotic Guardian campaign was developed, calling on health-care providers and the public to pledge to decrease antibiotic use. As of November, 2016, there were an estimated 34 496 pledges. A new programme launched in April, 2016, by the National Health Service England offers hospitals incentive funding to support pharmacists and clinicians for stewardship.

The University of Dundee and the British Society for Antimicrobial Chemotherapy collaboration with FutureLearn has developed an open-ended online course in stewardship, relevant to global health economies. More than 15 000 learners have registered in the first completed cycle, 34% of whom are not health-care providers, showing the ability of an online course to engage the public in antibiotic stewardship. Additionally, an infographic targeting health-care providers and the public using a superhero figure striking back against antibiotic resistance is innovative in raising antibiotic resistance awareness and education.

To engage prescribers, better access to routine data and strong leadership are key. In Scotland, a unique infection intelligence platform that links routinely collected clinical and laboratory data has been developed to understand the intended and unintended consequences of stewardship interventions, and inform clinical decision making at a population and clinical level, highlighting the value of informatics to support stewardship.

In England, a new antibiotic portal has been developed to centralise data and allow open access to data of local and national use, resistance, and stewardship, which replaces traditional paper-based reports. Scotland has developed a system where use and resistance data are regularly fed back to the stewardship team, who are encouraged to share this with prescribers and also use them as part of ongoing, clinically-focused educational activity.

Future directions
Several steps are being taken to advance stewardship, including promotion of effective sepsis management and development of performance metrics, and the development of electronic health records within secondary care hospitals—which together with mobile technologies and clinical decision support systems will hopefully enable stewardship opportunities and improve data linkage. National targets for England have been proposed to reduce total antibiotic use.

United we stand, divided we fall
High-level collaboration to drive the response to antibiotic resistance is being done by international organisations—eg, the tripartite alliance (WHO, World Organisation for Animal Health, and Food and Agriculture Organization)—bringing antibiotic resistance to greater prominence at a country level, through the Global Health Security Agenda, and between countries towards achieving sustainable outcomes from the UN General Assembly High Level
Meeting on antibiotic resistance in September, 2016. In this Personal View, we have highlighted antimicrobial stewardship road maps from five different countries. We have shown that although each country’s approach to antimicrobial stewardship is different, when nurtured, individual efforts such as the USA–South Africa collaboration can positively affect local and national antimicrobial stewardship programmes. Personal relationships and willingness to learn from each other’s stewardship successes and failures continues to foster collaboration. Individual stewards provide the day-to-day stewardship interventions, oversight, and education to assure appropriate antibiotic use. Global collaboration by any steward can occur through spreading awareness of the free publicly available online stewardship courses, the use of Twitter to connect and learn from experts globally, mentoring programmes, and research and publications. We summarise the key points and next steps in the panel.

All health-care providers who prescribe antibiotics need to take ownership, engage in stewardship, and understand the societal burden of inappropriate antibiotic use. To paraphrase Neil Armstrong, if antibiotic stewards worldwide join together and take “one small step” now, it will be a “giant leap for mankind” in the fight against antibiotic resistance.

Contributors

DAG and RK contributed equally to all phases of manuscript generation, from concept to literature search, writing, and review of the manuscript. EJCG contributed to the US section and review of the manuscript. DN and MG contributed to the UK component and review of the manuscript. KE-V and MVV contributed to the Colombia section and review of the manuscript. ACC and KAC contributed to the Australia section and review of the manuscript. AB, DaVB, and MM contributed to the South Africa section and review of the manuscript.

Declaration of interests

DAG, EJCG, DaVB, MM, AB, DN, ACC, KAC, and KE-V declare no competing interests. RK is employed by Merck & Co. The views expressed by RK are her own and not those of Merck & Co. MG is affiliated with the National Institute for Health Research (NIHR) Health Protection Research Unit (HPRU) in Healthcare Associated Infection and Antimicrobial Resistance at Imperial College London in partnership with Public Health England (PHE), and the NIHR Imperial Patient Safety Translational Research Centre. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, the Department of Health or Public Health England. MVV reports grants and personal fees from MSD; and grants from Pfizer, AstraZeneca, and Merck & Co outside the submitted work.

References


Panel: Next steps for global antibiotic stewardship collaboration

• Global antibiotic stewardship starts with individual stewards reaching out to each other to share experiences, education, and resources; to collaborate in research and publication; and to set up mentoring programmes
• Antibiotic policies to optimise antibiotic use are not enough; individual stewards need to have a global perspective and contribute to coordinating activities
• Although each country’s approach to antimicrobial stewardship is different, and when nurtured, individual effort can positively affect local and national antibiotic stewardship programmes
• Antibiotic stewardship models need to evolve from infection specialist-based teams to develop and use cadres of health-care professionals—including pharmacists, nurses, and community health workers—to meet the needs of the global population
• All health-care providers who prescribe antibiotics should take ownership and understand the societal burden of suboptimal antibiotic use

www.thelancet.com/infection  Published online November 17, 2016  http://dx.doi.org/10.1016/S1473-3099(16)30386-3


Torres JA, Tafur JD, Briceno DF, Pacheco R, Villegas MV. Generic antibiotics are a risk factor for mortality in Acinetobacter baumannii infections in Colombian ICUs. 49th ICAAC; San Francisco, CA, USA; Sept 12–15, 2009. K-312.


Australian Pesticides and Veterinary Medicines Authority. Quantity of antimicrobial products sold for veterinary use in Australia. Canberra: Australian Pesticides and Veterinary Medicines Authority, 2014.


