Improving the quality of antibiotic prescribing in the NHS by developing a new Antimicrobial Stewardship Programme: Start Smart—Then Focus

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There has been dramatic change in antibiotic use in English hospitals. Data from 2004 and 2009 show that the focus on reducing fluoroquinolone and second- and third-generation cephalosporin use seems to have been heeded in NHS secondary care, and has been associated with a substantial decline in hospital Clostridium difficile rates. However, there has been a substantial increase in use of co-amoxiclav, carbapenems and piperacillin/tazobactam. In primary care, antibiotic prescribing fell markedly from 1995 to 2000, but has since risen steadily to levels seen in the early 1990s. There remains a 2-fold variation in antimicrobial prescribing among English General Practices. In 2010, the NHS Atlas of Variation documented a 3-fold variation in the prescription of quinolones and an 18-fold variation in cephalosporins by Primary Care Trusts across England. There is a clear need to improve antimicrobial prescribing. This paper describes the development of new antimicrobial stewardship programmes for primary care and hospitals by the Department of Health’s Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection: Antimicrobial Stewardship in Primary Care Initiative. The secondary care programme promotes the rapid prescription of the right antibiotic at the right dose at the right time, followed by active review for all patients still on antibiotics 48 h after admission. The five options available are to stop, switch to oral, continue and review again, change (if possible to a narrower spectrum) or move to outpatient parenteral antibiotic therapy. A range of audit and outcome tools has been developed, but to maintain optimal antimicrobial usage, monitoring of local and national quantitative and qualitative data on prescribing and consumption is required, linked to the development of key performance indicators in primary, secondary and tertiary care.

Keywords: antibiotic, NHS, antimicrobial stewardship programme

Introduction

Antimicrobial resistance (AR) is an important patient-safety and public-health issue.1 The number of infections due to antibiotic-resistant bacteria is growing, and the pipeline of new classes of antibiotics is very limited.2,3 The emergence of AR is linked to antimicrobial exposure,4–6 and the overall uptake of antibiotics in a population, as well as the way antibiotics are used by individuals, has been shown to affect AR.6,7 This was demonstrated in a recent meta-analysis that found strong evidence linking the prescribing of antibiotics in primary care to antimicrobial resistance in pathogens causing urinary, respiratory and skin infections in individual patients.6 The likelihood of isolating resistant bacteria from a patient is strongly associated with the number and duration of antibiotic courses prescribed in the previous 12 months.6

Antimicrobial stewardship

Controlling AR requires a multifaceted approach. An antimicrobial stewardship programme (ASP) is an approach that can be used to improve antimicrobial prescribing and control antimicrobial resistance. An ASP describes a bundle of measures that can be
adopted to promote the appropriate use of antimicrobials, including:

1. Evidence-based optimal standards for routine antimicrobial use, e.g. correct selection of agent, dose, route of administration and duration of therapy.
2. Ensuring competency and educational programmes for all staff that use antimicrobials.
3. Communicating antimicrobial issues to all stakeholders.
4. Auditing the impact and uptake of these processes.
5. Optimizing outcomes for patients who receive antimicrobials.

The principal aims of an ASP are to improve efficacy, minimize adverse effects and unintended consequences of antimicrobial use and limit the spread of AR. Infections caused by resistant organisms are associated with poorer clinical outcome (morbidity and mortality), prolonged hospital length of stay and higher overall costs, compared with infections caused by susceptible organisms.

ASPs also aim to improve the cost-effectiveness of antimicrobial therapy:

1. directly, by limiting the excess and inappropriate use of these agents and by promoting active intravenous-to-oral (iv-to-po) switch therapy thus reducing unnecessary antimicrobial costs, and
2. indirectly, by (i) reducing the risk of drug-related adverse events and their associated costs, and (ii) by promoting optimized and timely delivery of antimicrobials and thus reducing unwanted consequences such as sub-therapeutic dosing and treatment failure.

The Antimicrobial Stewardship subgroup (ASG) of the Advisory Committee on Antimicrobial Resistance and Healthcare-Associated Infection (ARHAI) was established in 2003 as part of the Specialist Advisory Committee on Antimicrobial Resistance (SACAR), to focus on the prudent prescribing of antimicrobials across the National Health Service (NHS). The group’s remit is outlined in Figure 1.

- Promote the development of antimicrobial stewardship programmes by providing tools including the Antimicrobial Prescribing Framework and Self-assessment Toolkit (ASAT).
- Define safe and optimal antimicrobial usage by identifying national quantitative and qualitative data required on antimicrobial prescribing and consumption for Key Performance Indicators (KPIs) in primary, secondary and tertiary care. The ASG remit is to evaluate all current prescribing and antimicrobial consumption reporting systems with the aim of producing recommendations for a standardized uniform antibiotic consumption reporting system with the capability to interface with systems collecting clinical outcome data. Such a system would allow for more accurate, real, patient-linked data which could be used to promote good antimicrobial prescribing both locally and nationally and allow for benchmarking.
- Collaborate with major stakeholders in bringing about quality improvement in antimicrobial prescribing e.g. working with the Care Quality Commission to create assessment tools and working with the British National Formulary to improve the evidence base of antimicrobial prescribing guidelines.
- Provide advice and direction on research in antimicrobial prescribing.
- Act as a key liaison group, working with other relevant ARHAI and Health Protection Agency subgroups as well as key external stakeholders.

Figure 1. Remit of the Antimicrobial Stewardship Subgroup of the Advisory Committee on Antimicrobial Resistance and Healthcare-Associated Infection.

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National strategies to improve antibiotic prescribing

Over the last decade, there have been several initiatives to promote prudent use and prescribing of antimicrobials within England, and in order to support these national initiatives, ASPs are now included within regulatory frameworks. These initiatives, together with official texts and guidance from the Department of Health and national bodies to improve antibiotic prescribing, are summarized in Table 1. Criterion 9 of The Health and Social Care Act 2008: Code of Practice on the prevention and control of infections and related guidance8 outlines the guidance for compliance for registered organizations to provide evidence of prudent prescribing and antimicrobial stewardship. The Guidance for compliance with criterion 9 state: ‘Procedures should be in place to ensure prudent prescribing and antimicrobial stewardship. There should be an ongoing programme of audit, revision and update. In healthcare this is usually monitored by the antimicrobial management team or local prescribing advisors’.

It is important that all healthcare providers ensure that an ASP is in place. Surveys have indicated that up to 50% of antibiotic use is inappropriate,9 leading to increased AR, lengthened hospital stays for patients and subsequently increased costs to patient, hospitals and commissioners.

Activities to support antimicrobial stewardship in England

Annual antibiotic awareness campaigns

The Department of Health has been running annual antibiotic awareness campaigns since 1999 with the aim of educating healthcare professionals and helping to reduce public expectation of a prescription for antibiotics for coughs and colds, and thereby supporting general practitioners (GPs) in their efforts to reduce antibiotic resistance and healthcare-associated infections.

A range of campaign materials is available to download at www.dh.gov.uk/antibiotics, and these include non-prescription pads, which GPs find useful as the patient has a physical reminder of why a prescription was not given. The materials, including posters and leaflets, are available to GPs, pharmacists and hospitals as a tool to help doctors and pharmacists raise the issue of resistance and to help ensure the public receive a consistent message from all professions. Since 2008, the campaign has been run each year to coincide with the European Antibiotic Awareness Day on the 18 November.

European Antibiotic Awareness Day (EAAD)

EAAD arose from a European Centre for Disease Control (ECDC) initiative in 2008. The aims of EAAD within England are listed in Figure 2. Although EAAD provides an annual focus for promoting prudent prescribing, other initiatives, especially for prescribing professionals, are required throughout the year. Promoting the prudent use of antibiotics is particularly important in primary care as 80% of antibiotics are prescribed within primary care settings.10 Approximately half of these are prescribed for respiratory tract infections (common cold, acute bronchitis and acute sinusitis), a high proportion of which are caused by viral pathogens. There is documented evidence that the use of antibiotics has limited value in these conditions, leading instead to adverse effects, increased consultations with doctors, increased cost, unwanted effects and risk of AR. In addition, antibiotic prescribing continues to increase in primary care, with a 30% increase in the average daily quantities since 2000.11

Studies indicate that prescriptions for antibiotics are sometimes driven by patient demand and diagnostic uncertainty. With increasing antibiotic resistance and a lack of new agents with enhanced efficacy, it is essential that prudent and responsible use of antibiotics is actively promoted, to enable patients to make the right choices and reduce demand on prescribers for antibiotics. Several studies have shown that effective communication with patients determines patient satisfaction, rather than receiving an antibiotic prescription.12 The national campaign materials help support the work of GPs to educate patients in this area.

European Surveillance of Antimicrobial Consumption (ESAC)

This Europe-wide data collection initiative was launched in 2001, and all EU member states have signed up to it. The European Centre for Disease Prevention and Control (ECDC) has now taken over this programme. Each member country has a national network of experts collecting data on antimicrobial usage, which is collated and used for analysis and annual reporting of consumption trends.13

Antibiotic Resistance and Prescribing in European Children (ARPEC)

APREC (www.arpecproject.eu) was launched in 2010 by the European Society of Pediatric Infectious Disease and is funded by the Directorate-General for Health and Consumers (DG SANCO) specifically to improve the quality of community and hospital antibiotic prescribing in children. The key aim of the project is to collect and then use local and regional data in educational initiatives focusing on improving prescribing.

Antimicrobial Self Assessment Toolkit (ASAT)

ASAT was developed through a National Pharmacy Reference Group (including ASG members) using an evidence-based approach of published information and national reports, to identify criteria for inclusion. The web-based toolkit offers a process-based checklist for hospitals to self-assess their levels of antimicrobial stewardship.

The ASAT is subdivided into domains that address a number of issues including: (i) antimicrobial management within the Trust—structures and lines of responsibility and accountability, high-level notification to the board; (ii) operational delivery of an antimicrobial strategy—operational standards of good antimicrobial stewardship; (iii) risk assessment for antimicrobial chemotherapy; (iv) clinical governance assurance; (v) education and training—training needs and delivery of education and training for all who issue, prescribe and administer antimicrobials; (vi) antimicrobial pharmacist—systems in place for ensuring their optimum use; and (vii) patients, carers and the public—information for the needs of patients, carers and the public.
<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Publication title</th>
<th>Focus</th>
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<td>1999</td>
<td>Department of Health</td>
<td>Resistance to antibiotics and other antimicrobial agents: action for the NHS following the government’s response to the House of Lords Science and Technology Select Committee report “Resistance to antibiotics and other antimicrobial agents”</td>
<td>Set out an action plan for the NHS, aimed at reducing the emergence and spread of antimicrobial resistance and its impact on the treatment of infection. Includes strategies to monitor and optimize antimicrobial prescribing by implementing antibiotic guidelines, supporting professional development on appropriate prescribing, reducing inappropriate prescribing and using clinical governance arrangements to support improved prescribing</td>
<td>Health Service Circular</td>
<td>(27)</td>
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<td>2000</td>
<td>Department of Health</td>
<td>UK Antimicrobial Resistance Strategy and Action Plan</td>
<td>UK action plan to reduced resistance</td>
<td>Guidance</td>
<td>(28)</td>
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<td>2003</td>
<td>Department of Health</td>
<td>Winning ways: Working together to reduce Healthcare Associated Infection in England</td>
<td>Set out for the first time a clear direction for the local NHS to reduced HCAIs. Includes seven action areas including prudent use of antibiotics</td>
<td>Guidance</td>
<td>(29)</td>
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<td>2003</td>
<td>Department of Health</td>
<td>Hospital Pharmacy Initiative for Promoting Prudent Use of Antibiotics in Hospitals.</td>
<td>Letter highlighting new funding for promoting prudent antibiotic prescribing through enhanced clinical pharmacy activity.</td>
<td>Chief Medical Officer Professional Letter</td>
<td>(30)</td>
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<td>2006</td>
<td>Department of Health</td>
<td>The Health Act 2006</td>
<td>Code of Practice for Prevention and Control of Healthcare Associated Infections. Requires all NHS trusts to have antimicrobial prescribing policies</td>
<td>Code of practice</td>
<td>(31)</td>
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<td>2007</td>
<td>Department of Health</td>
<td>Saving Lives: reducing infection, delivering clean and safe care</td>
<td>Provides the tools and resources for Trusts to achieve the legal requirement to meet Implementation of Code of Practice for Prevention and Control of Healthcare Associated Infections (Health Act 2006)</td>
<td>Guidance/Toolkit</td>
<td>(32)</td>
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<td>2007</td>
<td>Specialist Advisory Committee on Antimicrobial Resistance (SACAR)</td>
<td>Antimicrobial framework</td>
<td>A framework to support the safe and appropriate use of antimicrobials</td>
<td>Best practice, care guideline; journal article</td>
<td>(33)</td>
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National audits

Surveillance of antibiotic prescribing in hospitals in England

To assess the current surveillance of antibiotic prescribing in hospitals in England, a survey of antimicrobial pharmacists was undertaken in 2009. The aim was to assess what levels of antibiotic prescribing data were being collected in hospitals in England. Furthermore, it was hoped that this survey would highlight areas of common practice and identify where there was variation. A list of questions was devised based on the parameters set out by the Department of Health as recommendations on prudent antibiotic prescribing and the ASAT. The questionnaire was circulated via the UK Clinical Pharmacy Association (UKCPA) mailing system to all antimicrobial pharmacists in England. Individual e-mails were also sent to the antimicrobial pharmacists.

In 2009, there were 174 Trusts in England, with many of them having a designated lead pharmacist for antibiotics and infection control. Of the 174 Trusts, 47 responded to the survey—a response rate of 27%. The responses to each question are summarized in Figure 3. Of the Trusts that responded, only 10% had electronic prescribing. Over 80% of Trusts produce periodic quantitative antibiotic consumption reports, using a range of different methods. The most common method of expressing antibiotic consumption was as WHO-defined daily doses (DDD)/1000 occupied bed-days.

Although 60% of respondents stated that they measured their antibiotic usage based on directives, only 45% sent these reports to the relevant directorate as feedback. Finally, only 15% of Trusts linked their usage reports to infection rates.
It was clear from the short survey that surveillance of antibiotic consumption is recognized as an important tool in the repository of Trusts. However, there is a great deal of variation in how these data are acquired, processed and presented. Ultimately some of these problems are due to the many different pharmacy dispensing systems in operation in hospitals in England, and to the time constraints on staff that have to produce these often labour-intensive data. The results from some of the hospitals are encouraging, and with the increased implementation of electronic prescribing, antibiotic consumption reports may become more easily accessible. However, it is interesting that according to this survey, relatively few Trusts share these data with clinicians. Timely feedback of antibiotic consumption data that is easily understood by clinicians and managers may be a very useful tool in encouraging prudent antibiotic prescribing and highlighting areas that require improvement.

**Survey of antimicrobial stewardship activities in English hospitals**

A survey of antimicrobial stewardship activities in English hospitals has recently been completed in collaboration with Imperial College and Imperial College Healthcare NHS Trust. The results will be published in 2012.

**Monitoring antibiotic consumption data**

**Primary care**

Data from the NHS Business Service Authority on prescriptions dispensed in England show a concerning trend in the total usage of antimicrobials from 1995 to 2009 (Figures 4 – 6). Although antibiotic consumption fell between 1995 and 2000, this has been followed by a steady rise in the prescription of antibiotics to both adults and children in primary care since then. This is despite National Institute for Health and Clinical Excellence (NICE) guidance to prescribers to avoid or delay prescribing for upper respiratory tract infections wherever possible. On a more positive note, over the more recent years there appears to be a proportional reduction in the prescribing of cephalosporins and fluoroquinolones (Figures 5 and 6).

**Variation in primary care prescribing**

There was a two-fold variation in antimicrobial prescribing for English GPs between the 10th and 90th percentiles of a 2009 sample (0.48 versus 0.95 antibiotic prescriptions per antibiotic STAR-PU (specific therapeutic group age–sex weightings-related prescribing unit)). Practice and practice population characteristics explained about one-sixth of the variation in antimicrobial prescribing nationally. Location of practice in the North of England was the strongest predictor of high antimicrobial prescribing. Practices serving populations with greater morbidity and those with a higher proportion of white patients prescribed more antimicrobials, as did practices with shorter appointments, non-training practices, and practices with higher proportions of GPs who were male, 45 years of age and qualified outside the UK. In 2010 the NHS Atlas of Variation documented a 3-fold variation in the prescription of quinolones and an 18-fold variation in cephalosporin prescription by Primary Care Trusts (PCTs) across England.

A recent IMS Health Mediplus database search of antibiotic prescribing rates and associated clinical indications in 0–18-year-old patients between 1996 and 2006 in the UK also found that prescribing declined by 24% between 1996 and 2000 but increased again by 10% during 2003–06. Antibiotic prescriptions for respiratory tract infections had decreased by 31% (P=0.01) mainly because of reduced prescribing for lower respiratory tract infections, tonsillitis and otitis. However GP prescribing for non-specific upper respiratory tract infections increased 4-fold (P=0.001), suggesting that GPs may be avoiding using diagnoses where formal antimicrobial guidance states that prescribing is not indicated.
Secondary care

National data for antimicrobial usage in secondary care have always proved difficult to obtain. In the UK, hospital pharmacy computer systems provide their issue data to IMS, who are the world’s leading source of information and analytics for pharmaceuticals. Data from IMS offer the most comprehensive analysis to date.

Total usage of antimicrobials in secondary care in England has shown only a slight increase, despite a 14.3% increase in the number of hospital admissions between 2004 and 2009 (data...
during this period, there was a 40% decline in the use of fluoroquinolones, a 50% decline in second-generation cephalosporin usage, a 22% decline in third-generation cephalosporin usage, but a 50% increase in carbapenem usage, a 3-fold increase in piperacillin/tazobactam usage (Figure 8) and a 50% increase in co-amoxiclav usage (Figure 9).

Thus, the national guidance of reducing the selection and use of fluoroquinolones and second- and third-generation cephalosporins appears to have been followed in secondary care. Indeed, this reduction in prescribing fluoroquinolones and second- and third-generation cephalosporins has been associated with a substantial decline in hospital *Clostridium difficile* rates.

There is, though, a need to report and analyse data at the hospital level in a way that will allow assessment of the effect of interventions using Effective Practice and Organization of Care (EPOC) methodology. An automatic electronic collection of antimicrobial usage system that utilizes the data files held on each hospital pharmacy computer would be a very useful tool for analysis and would enable data to be aggregated at a regional and national level. Patient-linked data will become more widely available as electronic prescribing and administration systems are slowly put in place. Given the importance of linking susceptibility reports and clinical diagnostic data, these developments are eagerly awaited.
and Infection Group, Health Protection Scotland and Public Health Wales. Other members of ARHAI (NHS Information Centre for Health and Social Care, GPs, pharmacists and microbiologists) have contributed. The ASPIC group has agreed that the most important indicator of good antimicrobial stewardship is total antibiotic use measured in items (STAR-PU), with a target initially set below the national 25th percentile on a set date. Indicators of good practice can be a real driving force for modifying behaviour, and these have been used very effectively in reducing methicillin-resistant Staphylococcus aureus (MRSA) and Clostridium difficile rates in the hospital setting.

Antimicrobial stewardship in secondary care

In 2009, the Department of Health in consultation with stakeholders developed a draft antimicrobial care bundle (High Impact Intervention) to outline an approach to safe and rational antimicrobial prescribing in healthcare settings and a method for auditing it. This has been revised, and, from November 2011, superseded by ARHAI guidance on antimicrobial stewardship under the title ‘Start Smart—Then Focus’, which aims to encourage clinicians to:

- initiate prompt effective antibiotic treatment within 1 h (or as soon as possible) in patients with life-threatening infections.
- document on drug chart and in medical notes: route, indication, dose, duration (RIDD).

Antibiotics in hospitals are often continued unnecessarily because clinicians caring for the patient do not have information indicating why the antibiotics were initially commenced and how long they were planned to be continued. This challenge is compounded where primary responsibility for patient care is transferred from one clinician to another. Ensuring that all antibiotic prescriptions are always accompanied by an indication, the correct dose and a clear duration will help clinicians change or stop therapy when appropriate.

Start Smart

- Obtain cultures first. Knowing the susceptibility of an infecting organism can lead to narrowing of broad spectrum therapy, changing therapy to effectively treat resistant pathogens and stopping antibiotics when cultures suggest an infection is unlikely.
- Prescribe: single dose for surgical prophylaxis where antibiotics have been shown to be effective. Critical to this initiative is that the single dose is administered at around 60 min prior to surgical incision to enable peak blood levels to be present at the start of the surgical treatment.

Figure 8. Total fluoroquinolone, cephalosporin, carbapenem and antipseudomonal penicillin usage in English hospitals (Courtesy of IMS).

Figure 9. Total co-amoxiclav usage in English hospitals (Courtesy of IMS).
A repeat dose of antibiotic prophylaxis is required when the operation is longer than the half-life of the antibiotic. Antibiotic treatment (in addition to prophylaxis) should be given to patients having surgery on a dirty or infected wound.

References:

Then Focus
- Review the clinical diagnosis and the need for continuing antibiotics by 48 h. Make an active antimicrobial stewardship decision to either stop, switch, change, continue or move to outpatient parenteral antibiotic therapy (OPAT).
Antibiotics are generally started before a patient’s full clinical picture is known. By 48 h, when additional microbiology, radiographic and clinical information is available, it is important for clinicians to reevaluate why the therapy was initiated in the first place and to gather evidence on whether there should be changes to the therapy. A clear, active, antimicrobial stewardship decision should then be made and documented in the notes for all patients on antibiotics (adults and children).

The five antibiotic stewardship decision options are Stop (stop antibiotics if there is no evidence of infection), Switch (switch antibiotics from intravenous to oral), Change (change antibiotics—ideally to a narrower spectrum, broader if required), Continue (continue and review again at 72 h) and OPAT (Figure 10a).

Figure 11. Key recommendations and future work plans.

Conclusions
Advocating patient safety and auditing of antimicrobial stewardship in hospitals should be based on the principles stated in these antimicrobial stewardship decision options. Examples of audit tools are shared in the full guidance.

An Antimicrobial Stewardship Forum which will include representatives of healthcare professionals and various stakeholders is currently being planned in collaboration with BSAC and HPA. The key recommendations and future work plans are shown in Figure 11.

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Members of the ARHAI Antimicrobial Stewardship Group. E. C. acknowledges support from the National Institute for Health Research

Figure 11. Key recommendations and future work plans.
TRANSPARENCY DECLARATIONS

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J. C.: Imperial College London, University of Manchester, Medicines and Healthcare Products Regulatory Agency, ARHAI. C. M. was a member of the NICE self-limiting respiratory tract infection guideline development group and leads the group that writes the HPA antimicrobial guidance for primary care. D. A. O. is also an Antimicrobial Pharmacist at Barking Havering and Redbridge University Hospitals NHS Trust. M. S. receives academic funding from a range of bodies including Pfizer, FP7, DG Sanco, NIHR, Action Medical Research, Sparks Charity. E. C. is an Academic Research Pharmacist at the National Centre for Infection Prevention and Management funded by UKCRC and NIHR BRC.

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