

REVIEW

# Antimicrobial Stewardship from Policy to Practice: Experiences from UK Antimicrobial Pharmacists

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## ABSTRACT

Antimicrobial stewardship in the UK has evolved dramatically in the last 15 years. Factors driving this include initial central funding for specialist pharmacists and mandatory reductions in healthcare-associated infections (particularly *Clostridium difficile* infection). More recently, the introduction of national stewardship guidelines, and an increased focus on stewardship as part of the UK five-year antimicrobial resistance strategy, have accelerated and embedded developments. Antimicrobial pharmacists have been

instrumental in effecting changes at an organizational and national level. This article describes the evolution of the antimicrobial pharmacist role, its impact, the progress toward the actions listed in the five-year resistance strategy, and novel emerging areas in stewardship in the UK.

**Keywords:** Antibiotic; Antimicrobial stewardship; Healthcare-associated infections; Pharmacy; Resistance

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## THE DEVELOPMENT OF ANTIMICROBIAL STEWARDSHIP IN THE UK: EARLY DAYS AND DRIVERS

In the early part of this century, the UK government focused heavily on reducing the incidence of healthcare-associated infections (HCAIs) [1, 2], such as methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremias and *Clostridium difficile* infections (CDI). A combination of voluntary, followed by mandatory, reporting of these infections allowed the National Health Service (NHS) to identify and monitor the scale of the problem, and then to develop actions to improve outcomes [3]. The peak incidence of MRSA bacteremias was seen in 2003, at 7700 cases, and for CDI the peak was seen in 2007, with 57,247 cases reported [4]. In response to these high levels, NHS hospital Trusts were set targets (with large financial penalties for failure) to reduce MRSA bacteremias by 50% by 2008 and CDI by 30% by 2010–2011 [5, 6].

At around the same time, antimicrobial stewardship (AMS) began to evolve rapidly when, in 2003, the Department of Health announced a three-year Hospital Pharmacy Initiative, complete with £12 million of funding for hospital pharmacies, aimed at improving the monitoring and control of anti-infectives [7], with a view to contributing to the efforts to tackle HCAIs. This thrust pharmacists into a key role in AMS with the majority of this money being spent creating antimicrobial pharmacist positions [8]. Immediate outcomes from this initiative were widespread update and revision of local antimicrobial guidelines, increasing interaction between Microbiology/Infectious Diseases and Pharmacy (leading to development of, or more frequent, joint ward rounds), and a dramatic

increase in the provision of education and training to healthcare professionals in prudent antimicrobial use [8, 9]. These interventions have been associated with improved antimicrobial usage, reductions in length of stay, and improved clinical outcomes (such as reductions in CDI) [10–14], and both of the high-level objectives for MRSA bacteremias and CDI cases were met with 57% and 41% reductions, respectively.

At the core of these reductions (most obviously for CDI) was improved antibiotic prescribing. Initial guidance documents around management of CDI recommended enhancing AMS, including: dedicated teams; using narrow spectrum antibiotics for empiric treatment where appropriate; avoiding the use of clindamycin and second- and third-generation cephalosporins, especially in the elderly; and minimizing the use of fluoroquinolones, carbapenems and prolonged courses of aminopenicillins [15–19]. Antimicrobial pharmacists have continued to play an integral role in developing and managing antimicrobial guidelines, reviewing individual patient regimens to optimize therapy, educating healthcare staff on the appropriate use of antimicrobials and monitoring and auditing outcomes of antimicrobial usage across organizations.

There has been a continued impressive 77% reduction in CDI cases from 108 cases per 100,000 population (in 2007–2008) to 25 cases in 2013–2014 [4]. Further developments in CDI objective setting now include a consideration of the avoidability of the case and whether there have been any “lapses in care” leading to the episode [20]. Although it is not discretely defined as such, inappropriate antimicrobial usage would be recognized as a “lapse in care”, and antimicrobial pharmacists continue to be heavily involved in optimizing therapy,

preventing CDI cases, and investigating them and sharing relevant learning when they occur.

In Scotland, similar targets, but without financial penalties, were set for the reduction of *S. aureus* bacteremia and CDI [21] which have resulted in similar significant reductions to those seen in England [22]. The national stewardship program led by Scottish Antimicrobial Prescribing Group (SAPG) has brought about reduced use of antibiotics associated with a high risk of CDI and this is acknowledged as a major factor in reducing the CDI rate [23].

## MORE RECENT DEVELOPMENTS IN UK STEWARDSHIP GUIDELINES AND STRATEGY

To better develop and standardise the stewardship strategy, official guidance and toolkits have recently been issued in the UK for community (primary) care in 2012 [24] and hospital (secondary) care, firstly in 2011 and very recently updated in 2015 [25, 26].

In 2013, a cross-government five-year antimicrobial resistance (AMR) strategy was published which takes a 'One Health' approach to tackling AMR [27]. This outlined seven key areas for action (Table 1) and recommended that, for the first time, an implementation plan and yearly progress reports be published. As healthcare in the UK is devolved into four different national services (England, Scotland, Wales and Northern Ireland) each nation has a committee, which oversees stewardship (Table 2). These groups are largely responsible for ensuring progress toward the AMR strategy and all have significant pharmacist input.

To date, antimicrobial pharmacists have had most involvement in three of the key areas

**Table 1** UK antimicrobial resistance strategy: seven key areas for action

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Better access to and use of surveillance data
Optimizing prescribing practice
Improving infection prevention and control
Improving professional education, training and public engagement
Improving the evidence base through research
Developing new drugs, vaccines and other diagnostics and treatments
Strengthening UK and international collaboration

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highlighted in the UK AMR strategy, which are discussed in detail below. Antimicrobial pharmacists have a smaller role in infection prevention and control by providing pharmaceutical expertise to infection control committees and infection prevention and control teams. Also, increasing work is being carried out to improve the evidence base through research into stewardship and to strengthen UK and international collaboration. Developing new compounds or vaccines for use in clinical practice, and the introduction of other diagnostics and treatments is usually beyond the remit of their work.

### Better Access To, and Use of, Surveillance Data

Feedback of consumption data is a key element of an AMS program [28]. In order to engage prescribers, data are needed [29] and lack of it is a barrier to effective implementation of AMS [30, 31]. In the UK, consumption data have been available since 1991 for community prescribers. It is captured as part of the reimbursement of community pharmacists for dispensing NHS prescriptions [32], but will not include antibiotics supplied by any other

**Table 2** National groups responsible for the overview of stewardship

Nation	Group	Date formed	Remit
England	Antimicrobial Stewardship subgroup (ASG) of the Advisory Committee on Antimicrobial Resistance and Healthcare-Associated Infection (ARHAI)	2003	Established 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)
	English Surveillance Program for Antimicrobial Utilization and Resistance (ESPAUR)	2013	Developed by Public Health England (PHE) to bring together antimicrobial utilization and resistance data, examine national implementation of stewardship initiatives and develop quality measures, methods to monitor unintended outcomes of antimicrobial stewardship and both public and professional behavior interventions
Scotland	Scottish Antimicrobial Prescribing Group (SAPG)	2008	To lead and coordinate delivery of the Scottish Management of Antimicrobial Resistance Action Plan (ScotMARAP) [83]
Wales	Welsh Antimicrobial Resistance Program Surveillance Unit (WARP-SU)	2008	Currently focuses on reporting antimicrobial usage and resistance data and coordinating nationwide antimicrobial audits
Northern Ireland	Antimicrobial Resistance Action Committee (ARAC)	2002	ARAC provides expert advice to the Department of Health, Social Services and Public Safety (DHSSPS) on all issues to do with antimicrobial resistance and provides leadership on strategies for tackling this issue. Strategy for Tackling Antimicrobial Resistance (STAR) 2012–2017 [84]

method, e.g. private prescriptions or packs given out in clinics. The data are used to compare rates of prescribing within localities using a standardized method to account for differences in the local population. For example, the use of Specific Therapeutic Group Age–sex weightings Related Prescribing Units (STAR-PU) as a denominator allows more accurate and meaningful comparisons within a specific therapeutic group by taking into account the types of people who will be receiving that treatment [33]. These data can be used to drive improvements in antimicrobial prescribing rates, total antibiotic consumption

and broad-spectrum antibiotic consumption (cephalosporins, fluoroquinolones and amoxicillin/clavulanate) [34, 35]. From 2005 until 2013, overall antimicrobial consumption had been increasing in the community, but significant reductions were seen in the use of cephalosporins and fluoroquinolones [32]. Although there has been no explicit linkage between increasing AMR rates and increasing consumption of specific antimicrobials or classes, in 2014, the Department of Health's expert advisory committee, the Advisory Committee on Antimicrobial Resistance and Healthcare Acquired Infections (ARHAI),

proposed that total antimicrobial consumption should reduce to 2010 levels in the community [36, 37] and that the proportion of antibiotics from cephalosporin, quinolone or amoxicillin/clavulanate classes should reduce by 10% from the 2013/2014 value or to less than the 2013/2014 median, whichever is the smaller reduction. In 2015–2016, a Quality Premium [38] (financial reward) was introduced to achieve this goal, along with a national reporting tool to monitor it [39].

In Scotland, a similar national quality indicator was introduced in 2013 aimed at reducing unnecessary antibiotic use for self-limiting respiratory infections. This uses a ‘best in class’ approach so that at least 50% of practices in each region will be at or below the 25th percentile of Scottish practices (using January–March 2013 as the baseline) or will have made the minimum acceptable reduction toward that level. In 2013–2014, there were 276,383 (6.5%) fewer prescriptions for systemic antibacterials in primary care in Scotland than in 2012–2013 and 57.5% of practices achieved the national quality indicator. Since 2008, there has been a focus on reducing the use of cephalosporins, quinolones and amoxicillin/clavulanate in the community and this has led to year-on-year reductions in the use of these agents [40].

For English hospitals, a detailed and comprehensive report published by the English Surveillance Program for Antimicrobial Utilization and Resistance (ESPAUR), set up by Public Health England in response to the five-year AMR strategy, provided the very first national data on antimicrobial consumption [41]. This report covered the period 2010–2013 and used consumption data derived from hospital pharmacy stock management systems for drugs dispensed to both individual patients and ward stocks. This type of data has to be used

because electronic prescribing (EP) in hospitals in England is very much in its infancy [41]. Using hospital pharmacy stock management systems prevents the reporting of detailed consumption data down to doctor or clinical team level, and neither of the two main pharmacy accounting systems used in the UK includes a reporting tool as standard. A worldwide survey of hospital AMS showed that 92% of UK hospitals reported antimicrobial usage data, but only 52% reported defined daily doses (DDDs) to specialty level, and even fewer were able to link consumption data to resistance or infection rates (31% and 33%, respectively) [42, 43].

The ESPAUR report [41] showed an increase in overall antibiotic consumption in hospital inpatients of 11.9% over the 4-year period (an average year-on-year increase of 3.5%, equivalent to 2.3–2.5 DDD per 1000 inhabitants per day). The data were reported at area level only, so did not allow benchmarking between hospitals.

ARHAI in England also proposed (although these proposals may be subject to further refinement) that total antibiotic consumption be reduced by 1% per annum over 2015–2019 (as measured by DDD per 1000 admissions per year), and total carbapenem consumption be reduced to 2010 consumption levels (as measured by the same method), corresponding to an average reduction of 20–25% [36, 37]. Again, there has been no explicit linkage between increasing antimicrobial consumption and increasing AMR, but the ESPAUR report does show increases in both elements over the reporting period, and controlling antimicrobial consumption is recognized as a key element of the AMR strategy [41]. In 2015–2016, consumption data are being validated by hospitals as part of the Quality Premium [38]. In addition, 65% of NHS hospitals are also using a specific software package (Rx-Info Define) to

benchmark hospital medicines consumption [44].

Since 2008, SAPG has published annual reports on antimicrobial use and resistance in humans [45] utilizing national data marts which collate data from hospital Pharmacy and Microbiology systems and prescriptions for antibiotics dispensed by community pharmacists. In Wales, the Welsh Antimicrobial Resistance Program Surveillance Unit (WARP-SU) [46] currently reports antimicrobial usage and resistance data. Finally, within Northern Ireland, the COMPASS system [47] provides data on primary care antibiotic prescribing with the national AMR dataset currently being developed.

### Optimizing Prescribing Practice

There are two national AMS toolkits for England: Start Smart then Focus for hospital care [25, 26] and the Treat Antibiotics Responsibly, Guidance, Education, Tools (TARGET) Antibiotics toolkit for community care [24]. Wales [48] and Scotland [49] have their own versions of the guidance. In addition, national guidance on AMS is due for publication in August 2015 by the National Institute for Health and Care Excellence (NICE) [50].

The Scottish Antimicrobial Prescribing Group has produced national guidance [49] on AMS and infection management to support antimicrobial teams and prescribers across hospital and community care settings. All regions have a centrally funded antimicrobial pharmacist position in addition to locally funded positions to support local delivery of stewardship and drive quality improvement in antimicrobial prescribing.

A large proportion of antimicrobial pharmacist time is currently dedicated to optimizing prescribing practice, as described later in this article.

### Improving Professional Education, Training and Public Engagement

Education and training is essential to optimizing prescribing and AMS, and, in order to drive consistency in practice, performance standards need to be set. The first national antimicrobial prescribing and stewardship competences were published in 2013 and these are currently being developed to include in Health Education England work streams [51]. The competences consist of five dimensions, and each dimension includes statements that describe the activity and outcomes that prescribers should be able demonstrate. The five dimensions are:

1. Infection prevention and control.
2. AMR and antimicrobials.
3. The prescribing of antimicrobials.
4. AMS.
5. Monitoring and learning.

Antimicrobial pharmacists are central to the delivery of education on stewardship for healthcare staff, and in 2014 an expert curriculum [52] was developed to support specialist Infectious diseases and antimicrobial pharmacists in this role, as well as providing professional development opportunities. The 4-year pharmacy degree contains variable amounts of teaching and training in AMS and there are limited postgraduate opportunities for pharmacists to gain specialist training in infection management and AMS [53]. The expert curriculum provides the first opportunity to develop some form of credentialing in this area.

The TARGET antibiotic toolkit [24] includes educational materials for prescribers in primary care. A similar initiative has also been developed in Wales: the 'Stemming the Tide of Antibiotic Resistance' educational program (STAR) [54, 55]. This includes resources for

clinicians to share with the public during consultations and is reported to have helped deliver changes in local prescribing practices and reduce unnecessary antibiotic use [56]. In Scotland, a similar program, the Scottish Reduction in Antimicrobial Prescribing (ScRAP) [57], was launched in October 2013 as an educational resource to help prescribers to meet a government target to reduce unnecessary prescribing of antibiotics. In 2015, SAPG, in collaboration with NHS Education for Scotland, launched a stewardship resource for nurses and midwives in the form of an interactive electronic workbook [58].

Since 2008, the UK has actively promoted ‘European Antibiotic Awareness Day’ (EAAD) which is held in November each year to raise awareness among health professionals and the public of AMR and appropriate prescribing and antimicrobial use. In 2014, to move from raising awareness to engagement, and as a marker for behavior change, a new campaign, Antibiotic Guardian, was developed which called on everyone in the UK to choose a

pledge on the website <http://www.antibioticguardian.com>. The pledges were developed using the behavior change strategy ‘if–then’ approach. In the first two months, 11,998 healthcare professionals and members of the public chose a pledge and became antibiotic guardians.

## HOW DOES THE PHARMACIST FUNCTION WITHIN STEWARDSHIP TEAMS?

In 2011, English hospitals reported employing an average of one full-time antimicrobial pharmacist per 776 inpatient beds, representing approximately 3% of the clinical pharmacists in those organizations [59]. These pharmacists vary in seniority, and often combine their antimicrobial duties with other responsibilities such as respiratory or intensive care specialist roles [59]. The typical activities of antimicrobial pharmacists in hospitals have been well described in the literature, and are shown in Table 3 [8, 9, 41, 59–62]. Key to all of

**Table 3** Typical activities of UK antimicrobial pharmacists

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Production and dissemination of evidence-based prescribing guidelines and prescribing policies, increasingly utilizing technology such as smartphone ‘apps’ and electronic training packages
Education of prescribers, pharmacy and nursing staff in the prudent use of antimicrobials, including mandatory induction training for all staff
Providing a clinical advice service, often with access via a pager, supporting prescribers in optimizing antimicrobial therapy for individual patients, and providing input on multidisciplinary infection ward rounds
Advising on therapeutic drug monitoring for antimicrobials
Monitoring and feedback of trends in antimicrobial prescribing, formulary and guideline adherence to clinical teams, and inputting into governance structures within organization. Point prevalence surveys of antimicrobial use, conducted at least annually, are widespread in the UK, though an increasing number of hospitals are using rapid feedback of quality indicator measures to drive improvements in antimicrobial prescribing [14]
Managing entry of new antimicrobials onto hospital formularies, including critical review of new agents and their place in therapy
Clinical research, both in support of drug registration studies, and in novel research to consolidate the evidence base around antimicrobial stewardship

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this activity is the well-established linkage between AMS pharmacists and their microbiologist/infectious diseases colleagues, which allows both specialties to share and contribute to optimizing patient care. Also, due to the patient load and their other responsibilities, antimicrobial pharmacists in the UK rely heavily on contributions from their hospital pharmacy colleagues to deliver the fundamentals of AMS (following appropriate education and training from the specialist pharmacists themselves), and also to identify patients that require more specialist input. However, although these activities are well-described, good-quality evidence of their impact on optimizing antimicrobial therapy and patient outcomes is sadly lacking. Improving this evidence-base forms one of the future aspirations of the specialty, utilizing upcoming developments in data capture to take this forward (see below).

In comparison to the hospital sector, there are very few dedicated antimicrobial specialist pharmacist roles in primary care in the UK. A survey carried out in 2014 identified that, in 66% of primary care organizations, AMS roles were led by generalist prescribing advisors/medicine management pharmacists [63]. AMS activities of pharmacists in primary care are similar to those in secondary care in respect to guideline writing, audit, education, monitoring and feedback; often teams link with hospital microbiology laboratories for clinical infection advice. Given that over 85% of antimicrobials are prescribed outside the hospital sector in the UK [41], and with the increasing emphasis on a 'One Health' approach to tackling AMR [27], cross-sector AMS programs, where primary and secondary care specialists work together to improve prescribing across a regional population, are likely to become the norm over the coming years. There are already some

examples of cross-sector working in select regions of the UK, where specialist antimicrobial pharmacists from both sectors work on collaborative projects to improve antimicrobial use.

In Scotland, antimicrobial pharmacists have a remit for hospital and community care and work closely with prescribing advisers to influence general practitioners antibiotic prescribing behaviors. The national network of antimicrobial pharmacists works closely with SAPG to support the national stewardship program and, in addition, they have their own annual work plan of quality improvement initiatives.

## THE CHANGING HEALTHCARE LANDSCAPE: AN OPPORTUNITY FOR ANTIMICROBIAL PHARMACISTS?

Creating national infrastructures and technologies to help support AMS development has been important for UK antimicrobial pharmacists and their teams. The tools already discussed have provided opportunities particularly at a local level for teams to review, develop, implement and encourage AMS strategies. However, the challenge is how to adapt local stewardship programs to the evolving, changing healthcare landscape that is the NHS. Below, are a few scenarios of where UK pharmacists are becoming involved in more novel stewardship activities.

### Electronic Systems

Although there is an extensive literature on the positive contribution that electronic systems (such as computerized clinical decision support,



computerized physician order entry or full EP) can provide to AMS, the bulk of this originates from the USA, South East Asia, and Australia, where such systems have been in use for many years [64–68]. EP is not yet widely implemented in the UK, although a handful of pathfinder hospitals have had experience with EP systems for a considerable time [69]. Furthermore, although the potential benefits from introduction of EP have long been recognized [70, 71], little work has so far been published on the actual impact of these systems on antimicrobial usage and resistance. Four small case studies have reported on the impact of electronic systems in AMS in the UK [72–75] demonstrating decreased levels of antimicrobial usage [72], increased identification of patients requiring intervention [73], avoidance of clinically significant drug interactions [74] and improvements in documentation of key antimicrobial indicators (such as indication and duration, which feature in the Start Smart, Then Focus toolkit) [75].

Around 15 different providers of EP systems are active within the UK market, and these products are being used in about 20% of NHS Trusts, with an expectation that 40–50% of Trusts will have a plan for implementation of EP in place by 2016 [76]. With this large number of different solutions and timelines for implementation, there will inevitably be significant variation in how EP is used to support AMS. There is an on-going research program investigating how EP is introduced into NHS Trusts which will include work looking at effectiveness (primarily safety considerations around drug–drug interactions or allergy awareness) and outcomes [76]. Work is beginning, with the formation of ESPAUR, to help guide NHS Trusts in their procurement and implementation plans for EP, with specific reference to their use in AMS. It is to be

expected that, as EP systems and their use in stewardship matures within the UK, an increasing evidence base will become available, highlighting additional beneficial outcomes (and potential pitfalls).

A further step change in the benefits of EP for stewardship will be achieved by implementation of mobile technologies harnessing EP, biochemical and microbiological results, patient observations, radiology, and clinical decision support in a single point-of-care device. There are a large number of antimicrobial smartphone apps available within the UK, commonly providing information on preferred antimicrobial choices for specific indications, but, as this field also matures, the exciting possibilities provided by linking these apps with the many data sources available to support clinical decision making will drive innovation and research in this area.

### **Antifungal Stewardship Initiatives**

Despite the low incidence of invasive fungal infections compared to bacterial infections, for some specialist centers antimicrobial expenditure is dominated by antifungal use. While strategies have focused on the prudent use of antibiotics, antifungal stewardship is less well defined. This is primarily due to a lack of effective diagnostics to guide therapy, of therapeutic drug monitoring to guide dosing and of knowledge of the funding arrangements for antifungals. Antifungal stewardship initiatives are gaining momentum in the UK at present with pharmacists driving the agenda. One such program [77] has suggested savings of approximately £180,000 over a 12-month period by rationalizing and reviewing therapies, while another two programs [77, 78] found stepping down and stopping unnecessary empiric therapy was common.

## Outpatient Parenteral Antimicrobial Therapy

Over recent years, there has been a drive to treat patients closer to their own home, facilitating early discharge or even avoiding admission altogether. For antimicrobials, outpatient parenteral antimicrobial therapy (OPAT) offers a safe and effective (clinically and financially) [79] means to deliver treatment outside the inpatient setting, providing good clinical governance and AMS practices are in place [80, 81]. Pharmacists have been cited as core members of the OPAT team in both the adult and pediatric UK OPAT good practice recommendations [81, 82]. This has led to a number of pharmacists taking national roles in this area, particularly addressing the stewardship dilemma that OPAT presents where the convenience of dosing antimicrobials to suit OPAT may take precedence over the spectrum of activity [80].

## SUMMARY

In summary, antimicrobial pharmacists in the UK have significantly increased in number and greatly contributed to large reductions in selected HCAIs over the last decade. They are also instrumental in meeting the actions set out by the UK AMR Strategy, with significant progress made toward several of the key areas for action. Improving the evidence base through research, developing novel stewardship strategies and strengthening national and international networks are areas where UK antimicrobial pharmacists must concentrate their efforts in the coming years. We look forward to working collaboratively with a wider, international, group of colleagues in the future.

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