ESPAUR 2016: antibiotic and antifungal prescribing in England

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The English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) was set up by Public Health England in 2013 in response to the government’s five-year antimicrobial resistance strategy in order to monitor antimicrobial use, resistance and stewardship across England. The key findings of their 2016 report show that some progress is being made, especially in primary care.

Apocalyptic events feature in the news almost daily – so frequently that we risk becoming blasé about our future health and security. But there is certainly no shortage of concern in government and healthcare circles about the impact of increasing antimicrobial resistance (AMR). Chief Medical Officer Dame Sally Davies has repeatedly warned that AMR is “the biggest threat to global health” that portends a return to an era when infection accounted for 40% of all deaths. The Review on AMR, chaired by Jim O’Neill, commissioned by the government to estimate the economic impact of AMR, states that by 2050, 10 million lives a year and a cumulative US $100 trillion of economic output are at risk due to the rise of drug-resistant infections if behaviour does not change.¹

A role of ESPAUR
The purpose of ESPAUR is to “develop, maintain and disseminate robust data for antimicrobial use (AMU), AMR and antimicrobial stewardship (AMS) implementation”; “enable optimum use of this data across healthcare settings”; and “measure the impact of AMU and AMS on AMR and patient safety”.

It has made surveillance data available via the Fingertips interactive web tool (https://fingertips.phe.org.uk), with six domains covering AMR, prescribing, infections and stewardship to foster greater awareness and facilitate local action plans. Data on 70 quality indicators can be viewed for CCGs, acute

Figure 1. Proportions of bloodstream isolates of E. coli nonsusceptible to the antibiotics indicated. From: Public Health England. ESPAUR. Report 2016²
trusts and primary care. The quality of data has been improved by increasing the proportion of NHS laboratories reporting AMR testing from 30% to 98%, and daily reporting from 10% to 82%. At the same time, routine antibiotic testing and interpretation of results has been standardised. Antibiotic prescribing can now be tracked by separate sectors, so prescribing by dentists and in independent hospitals can be scrutinised.

ESPAUR introduced the Antibiotic Guardian campaign to change behaviour among health professionals and the public (http://antibioticguardian.com). This programme of education and training engages with undergraduate and postgraduate educators, community pharmacy teams, healthcare students, schools, families and carers to encourage public debate. Work on stewardship includes assessing the use of toolkits supporting implementation in primary and secondary care and the introduction of a new toolkit for dentists. Fungal infections, once

Figure 2. Prevalence by quintile of E. coli isolates from blood resistant to (A) ciprofloxacin and (B) third-generation cephalosporins in CCGs across England, Q2 2016. From: Public Health England. ESPAUR. Report 2016.
### Infections

About half of *E. coli* bloodstream infections arise from urinary tract infections. Resistance rates for trimethoprim are now 16–67% (median 29%), with 86% of CCGs having rates greater than 25%. Nitrofurantoin is now the preferred treatment; resistance rates range from 0.3% to 13% (median 3.6%).

The annual incidence of tuberculosis in England in 2015 was 10.5 per 100,000; 72% of cases were people born outside the UK. Of the cases tested in that year, 7.4% were resistant to at least one front-line antibiotic but the prevalence of multidrug resistance has fallen since 2011 from 1.6% to 1.3%. Similarly, multidrug plus rifampin resistance is now less common (1.6%), though 23% of these cases were extensively resistant – that is, resistant to front-line drugs, at least one injected drug and at least one quinolone.

Cases of gonorrhoea resistant to penicillin, ciprofloxacin and tetracycline were so common that azithromycin and ceftriaxone became the treatments of choice. An azithromycin-resistant strain was detected in Leeds in 2015 and has subsequently spread throughout England, prompting increased surveillance and follow-up for test of cure and contact tracing.

The first case in the world of resistance to dual therapy with azithromycin/ceftriaxone was identified in England in 2015; the infection, acquired in Japan, fortunately responded to increased doses.

### Antibiotic consumption

Most antibiotic prescribing in England occurs in primary care (74%) followed by secondary care (inpatients 11%; outpatients 7%) and dental practice (5%). Total antibiotic prescribing has been decreasing slowly every year since 2012 and fell by 4.3% between 2014 and 2015. Most of this reduction was due to less prescribing in general practice (down 6.1%) and by dentists (down 6.9%) between 2012 and 2015. Hospital antibiotic prescribing was broadly stable between 2012 and 2015 but decreased between 2014 and 2015 by 8% for outpatients and by 2% for inpatients. “Other prescribers” in the community (mostly out-of-hours services) increased their prescribing by 11% between 2012 and 2013.

### Antibiotic resistance in England

The prevalence of resistance to commonly used antibiotics, at least in relation to bloodstream infections, was generally either stable or only a little worse between 2011 and 2015 (as exemplified by *E. coli* resistance rates – see Figure 1). The biggest changes have been an increase in resistance to co-amoxiclav among strains of *E. coli* (from 31% to 42%) and among *Klebsiella pneumoniae* (from 19% to 28%).

Hospitals have seen increasing resistance to piperacillin/tazobactam and the continued spread of *Klebsiella* spp. carrying carbapenemases (enzymes that confer resistance to the carbapenem antibiotics used to treat serious multidrug-resistant infection). Resistance to vancomycin among *Enterococcus* spp. increased from 10% to 16% between 2011 and 2015. There has been little change in resistance to penicillins and macrolides among *Streptococcus pneumoniae* and the slow decline in methicillin-resistant *Staphylococcus aureus* (MRSA) continues.

Between 2014 and 2015, the number of bloodstream infections due to *E. coli* or *K. pneumoniae* increased by 4.6% and 9% respectively, so the clinical burden of resistance actually grew. Infections are more common in the very young and elderly, though the patterns of resistance correspond with age less clearly (possibly due to differences in antibiotic utilisation). There is variation between CCGs in the prevalence of *E. coli* resistance to ciprofloxacin and third-generation cephalosporins, with broadly but not exclusively higher rates in areas of high population density (see Figure 2).

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**Figure 3.** Total antibiotic consumption by key antibiotic groups, expressed as Defined Daily Doses (DDD) per 1000 inhabitants per day, England, 2010–2015. From: Public Health England. ESPAUR. Report 2016.
2015, though this accounted for less than 4% of total antibiotic use.

Figure 3 shows prescribing rates for the major classes of antibiotics. Patterns of use have changed little between 2010 and 2015, with penicillins (45%), tetracyclines (22%) and macrolides (15%) accounting for most prescriptions in 2014. The use of penicillins decreased by 7% between 2012 and 2015, largely due to less prescribing of amoxicillin by GPs. There has been a large fall in the use of oral cephalosporins whereas prescribing of the parenteral ceftriaxone has increased, possibly due to increased use in home and other nonhospital settings.

Primary care accounts for 90% of tetracycline prescribing, over 80% of which is of doxycycline and tetracycline to treat acne. Use of these agents has increased since 2010 whereas minocycline and oxytetracycline are now much less frequently prescribed. By contrast, quinolone prescribing has been falling for several years, with only levofloxacin bucking the trend with a 54% growth since 2012.

Prescribing of macrolides decreased by nearly 6% since 2012, due largely to less use of erythromycin; this was partly offset by more use of azithromycin (especially for COPD exacerbations) and clarithromycin.

The greatest reduction in antibiotic use has been for treating respiratory tract infections (see Figure 4). Most of this fall is due to less use of amoxicillin. The majority of prescriptions issued by dentists are for amoxicillin and metronidazole and prescribing of both fell between 2011 and 2015.

The Quality Premium was introduced in 2015/16 to encourage CCGs to reduce their antibiotic prescribing. The targets were to reduce total prescribing by 1% from the 2013/14 level and to cut the proportion of prescriptions for co-amoxiclav, cephalosporins and quinolones by 10% or below the national median. Over 12 months, 201 of 208 CCGs reduced their antibiotic prescription items (from a median of 1.188 to 1.087 items per Specific Therapeutic group Age-sex Related Prescribing Unit; STAR-PU) and 189 of 209 CCGs met the target to reduce their use of broad-spectrum antibiotics (median reduction from 10.8% to 9.6%). There was, however, a two-fold difference in the performance of low- and high-prescribing CCGs.

In hospitals, antibiotic prescribing had been rising until 2014. In the following year, volume fell by 5%, largely thanks to the efforts of teaching hospitals. However, prescribing in large and medium trusts was unchanged and usage increased in smaller centres. ESPAUR speculates that stewardship initiatives were taking effect in larger institutions and longer durations of stay were exacting a toll in smaller units.

The greatest threat in secondary care is posed by multidrug resistant Gram-negative bacteria. Prescribing of carbapenems has been rising since 2010 (though it has since fallen in teaching hospitals), as has piperacillin/tazobactam (up 62% since 2010) and colistin (up 30% since 2013), which are used to treat infection by carbapenem-resistant organisms.

**Antifungal resistance, prescribing and stewardship**

The increasing complexity of medical interventions, particularly in transplant surgery and the use of immunosuppressive therapies, means more patients are at risk of fungal infection. ESPAUR notes growing evidence of invasive fungal disease, reports of more intrinsically resistant species of fungi, and cross-resistance to azoles and broad-spectrum antifungals.

Aspergillosis and fusariosis are the two commonest invasive fungal infections and the incidence of both has been rising slowly over the past five years. The reported rate of resistance to azole antifungals among Aspergillus fumigatus is erratic but in 2015 was 8%, down from a peak of 20% in 2013. Azole resistance among Fusarium spp. is more substantial, rising from 17% in 2011 to 65% in 2015. Candida spp. was implicated in 1.5% of bloodstream infections in 2014, ranking 11th among all pathogens. The incidence of candidaemia has been increasing since 2008. Resistance to azoles and caspofungin is low among C. albicans but up to 50% of Candida glabrata strains are reportedly resistant to azoles. The multiresistant Candida auris has emerged as a growing threat in hospitals since 2009.

Almost all antifungal prescribing takes place in primary care and most of this is for terbinafine, with fluconazole and itraconazole making up most of the remainder. Prescribing volume has fallen by 13% since 2013 but these agents are available over the counter and ESPAUR takes no account of this use. Antifungal use in hospitals decreased by 4%, with all agents except fluconazole seeing a fall. Of 47 NHS trusts responding to a survey, 11% said they had a specific anti-
fungal stewardship programme, 43% said it was part of their overall antimicrobial strategy, and 26% had no programme but monitored usage. Of 21 trusts commenting on barriers to antifungal stewardship, two-thirds cited lack of staff time.

Antibiotic stewardship

ESPAUR has supported and encouraged stewardship in dentistry, community and mental health services, and primary and secondary care. Its analyses suggest generally favourable outcomes, though community health service trusts seem to be falling short on measures to optimise antibiotic prescribing, with patchy training provision and variable implementation of toolkits. In primary care, the RCGP TARGET antibiotics toolkit website received an average of 6000 hits per month in 2015/16; half of the 1415 users of the AMR module reported undertaking an antibiotic audit in the last two years.

AMR was introduced as a national Commissioning for Quality and Innovation (CQUIN) target for secondary care in April 2016. Initial returns from 125 trusts show that the proportion of antibiotic prescriptions with a documented indication averaged 88% but ranged from 29% to 100%; the proportion reviewed within 72 hours was 81% (range 22%–100%).

Summary

The Department of Health and PHE are implementing a massive campaign to tackle antimicrobial resistance that appears to be getting results. Multiresistant bacteria remain a concern in secondary care but elsewhere, with the possible exception of community health services, the tide of neglectful antibiotic use may be on the turn.

References


Declaration of interests

None to declare.

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