Antimicrobial stewardship: prescribing antibiotics

Key therapeutic topic
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Options for local implementation

- Antimicrobial resistance poses a significant threat to public health, especially because antimicrobials underpin routine medical practice.

- Review and, if appropriate, revise prescribing and local policies that relate to antimicrobial stewardship to ensure these are in line with NICE guidelines on antimicrobial stewardship: systems and processes for effective antimicrobial medicine use and antimicrobial stewardship: changing risk-related behaviours in the general population.

- Review and, if appropriate, optimise current prescribing practice and use implementation techniques to ensure prescribing is in line with NICE antimicrobial prescribing guidelines or Public Health England (PHE) guidance on managing common infections in primary care, the Department of Health's guidance Start smart – then focus, local trust antimicrobial guidelines and the Antimicrobial Stewardship in Primary Care collaboration TARGET antibiotics toolkit.

- A national programme to reduce inappropriate antibiotic prescribing is in place through the Commissioning for Quality and Innovation (CQUIN) and the Quality Premium schemes.

- Promote the antibiotic guardian call to action and the keep antibiotics working campaign.
Evidence context

Antimicrobial resistance and stewardship

Antimicrobial resistance poses a significant threat to public health, especially because antibiotics underpin routine medical practice. The Chief Medical Officer’s report on the threat of antimicrobial resistance and infectious diseases (2013) highlights that, although a new infectious disease has been discovered nearly every year for the past 30 years, there have been very few new antimicrobials developed. This is leaving the armoury nearly empty as diseases evolve and become resistant to existing antimicrobials. The report highlights that looking after the current supply of antimicrobials is equally as important as encouraging development of new drugs.

A practical example of this is given in the English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report 2016. Rates of Escherichia coli (E. coli) and Klebsiella pneumoniae (K. pneumoniae) bloodstream infections increased by 15.6% and 20.8% respectively from 2010 to 2014 and further increases of 4.6% and 9% respectively were seen from 2014 to 2015. The 2017 ESPAUR report stated that the proportion of E. coli bloodstream infections resistant to piperacillin/tazobactam (the most frequently used antibiotic for the treatment of sepsis) increased year on year between 2012 and 2015, from 9.6% to 11.6%, but showed a smaller increase in 2016 to 11.8%. For K. pneumoniae bloodstream infections resistant to piperacillin/tazobactam, there was an increase between 2012 and 2015 from 13.3% to 18.6%, and a slight decrease to 17.8% in 2016. The 2016 report states that increases in resistance to piperacillin/tazobactam will increase the pressure on clinicians to use carbapenems (which are the antibiotics of last resort) unless alternative treatment strategies are developed.

For some other bacteria where there have been targeted interventions to reduce the burden of infection or resistance, infection rates or proportions of infections where resistance is detected have declined. For example, according to the ESPAUR report 2015, methicillin-resistant Staphylococcus aureus (MRSA) bloodstream infections had reduced from 12% to 8% over the previous 5 years through effective infection prevention and control within healthcare settings.

NICE has published a guideline on antimicrobial stewardship: systems and processes for effective antimicrobial medicine use. This recommends that commissioners should ensure that antimicrobial stewardship operates across all care settings. They should consider including the following in their antimicrobial stewardship programme:

- monitoring and evaluating antimicrobial prescribing and how this relates to local resistance patterns
• providing regular feedback to individual prescribers in all care settings about their antimicrobial prescribing and patient safety incidents related to antimicrobial use

• providing education and training to health and social care practitioners about antimicrobial stewardship and antimicrobial resistance

• integrating audit into existing quality improvement programmes.

NICE has also published a guideline on antimicrobial stewardship: changing risk-related behaviours in the general population. Public Health England (PHE) has published an antimicrobial resistance resource handbook, which collates national resources on antimicrobial resistance, antimicrobial stewardship and infection prevention and control. NHS England has also collated information on addressing antimicrobial resistance. Resources include 2 national toolkits to support implementation of antimicrobial stewardship best practice: the TARGET antibiotics toolkit for primary care and ‘Start smart, then focus’ for secondary care. A dental antimicrobial stewardship toolkit is also available.

The ESPAUR report 2017 states that almost 43,000 people have become antibiotic guardians. Becoming an antibiotic guardian involves pledging an action to reduce the unnecessary use of antimicrobials and is open to members of the public and healthcare professionals. Public Health England has also launched the national public campaign, Keep Antibiotics Working, to support the government's efforts to reduce inappropriate prescriptions for antibiotics by raising awareness of the issue of antibiotic resistance and reducing demand from the public.

**Antibiotic prescribing**

To help prevent the development of resistance it is important to prescribe antibiotics only when they are necessary, and not for self-limiting mild infections such as colds and most coughs, sinusitis, earache and sore throats. For example, the NICE antimicrobial prescribing guideline on acute sinusitis recommends no antibiotics for people presenting with symptoms for around 10 days or less. PHE guidance on managing common infections in primary care recommends that consideration should be given to a no, or back-up (delayed) antibiotic strategy for acute self-limiting upper respiratory tract infections and mild urinary tract infections (UTIs). It also advises that people should be given supporting information about antibiotic strategies, infection severity and usual duration, such as treating your infection leaflets.

When antimicrobials are necessary to treat an infection that is not life-threatening, a narrow-spectrum antibiotic should generally be first choice. Indiscriminate use of broad-spectrum antibiotics creates a selective advantage for bacteria resistant even to these 'last-line' broad-
spectrum agents, and also kills normal commensal flora leaving people susceptible to antibiotic-resistant harmful bacteria such as *Clostridium difficile* (*C. difficile*). For infections that are not life-threatening, broad-spectrum antibiotics (for example, co-amoxiclav, quinolones and cephalosporins) need to be reserved for second-choice treatment when narrow-spectrum antibiotics are ineffective (*Chief Medical Officer Annual report 2011*).

Addressing healthcare-associated *C. difficile* infection remains a key issue on which NHS organisations have been mandated to implement national guidance. The Department of Health and PHE report on *Clostridium difficile infection: how to deal with the problem* from 2008 recommends that trusts should develop restrictive antibiotic guidelines that use narrow-spectrum agents alone or in combination as appropriate. The report suggests that these guidelines should avoid recommending clindamycin and second- and third-generation cephalosporins (especially in older people) and should recommend minimising the use of quinolones, carbapenems (for example, imipenem and meropenem) and prolonged courses of aminopenicillins (for example, ampicillin and amoxicillin). Broad-spectrum antibiotics should be used only when indicated by the person’s clinical condition, and their use should be reviewed after the results of microbiological testing or based on the sensitivities of causative bacteria.

The Department of Health Advisory Committee on *Antimicrobial Prescribing, Resistance and Healthcare Associated Infection* (APRHA) recommends the *Start smart – then focus* approach. This advises that, if immediate antibiotic treatment is necessary, the clinical diagnosis and continuing need for antibiotics should be reviewed within 48–72 hours. A study of Start smart – then focus, which was discussed in a NICE eyes on evidence article on *implementation of antibiotic prescribing guidance*, concluded that most hospital antibiotic policies in England ‘start smart’ by recommending broad-spectrum antibiotics for empirical therapy in severe infections. However fewer ‘focus’ by reviewing the ongoing need for antibiotics after a couple of days, as recommended.

A NICE evidence summary on *Clostridium difficile infection: risk with broad-spectrum antibiotics* reviews the evidence on this infection. It concludes that meta-analyses in people with hospital-associated and community-associated *C. difficile* infection confirmed that the antibiotics most strongly associated with the infection were clindamycin, cephalosporins and quinolones. However, the interpretation of data on the risk of *C. difficile* with different antibiotics is extremely difficult. Such data should be interpreted with caution and should not be considered to definitively show which antibiotics or subgroups of antibiotic classes carry higher risks of *C. difficile* infection. Although the data have limitations that prevent firm conclusions, the evidence shows the importance of following antibiotic guidelines that recommend that all broad-spectrum antibiotics are prescribed appropriately and with careful stewardship.
According to PHE guidance on managing common infections in primary care, cefalexin, other cephalosporins (cefixime, cefotaxime and ceftriaxone) and quinolones (for example, ciprofloxacin and ofloxacin) should be used only in limited situations. The ESPAUR report 2017 found that broad-spectrum antibiotic use continues to decrease in primary care. However, despite low levels of use and resistance, the proportion of bloodstream infections resistant to third-generation cephalosporins and ciprofloxacin has not changed significantly in the last 5 years.

Although identifying cephalosporins and quinolones as 'high-risk' may have been an important control measure in reducing the risk of C. difficile infection, an unintended consequence of this may have been an increase in clinically inappropriate prescribing of co-amoxiclav and other broad-spectrum antibiotics, such as piperacillin-tazobactam, carbapenems and co-trimoxazole. According to PHE guidance on managing common infections in primary care, these antibiotics have a very limited set of recommended clinical indications.

The ESPAUR report 2017 found that the use of co-amoxiclav is now declining. There was a decrease of 5.4% between 2015 and 2016 in the use of co-amoxiclav; and bloodstream infections resistant to co-amoxiclav, which were increasing until 2015, decreased slightly in 2016. Until 2015, hospitals were continuing to increase their use of the antibiotics of last resort (piperacillin/tazobactam, carbapenems and colistin). However, from 2015 to 2016 hospitals reduced their use of piperacillin/tazobactam and carbapenems (both by approximately 4%), which is the first step in reducing antibiotic use in hospitals.

An audit and questionnaire survey to establish what proportion of sickness policies of UK childcare providers comply with PHE guidance, discussed in NICE's medicines evidence commentary on infective conjunctivitis: do childcare provider policies help drive inappropriate prescribing of antimicrobials?, found that only 13% of childcare provider policies reflected PHE advice and almost half required treatment with antibiotics before the child could be readmitted to nursery. In a questionnaire survey of primary care prescribers, about 40% said that childcare provider policy had been the main or only reason for prescribing topical antibiotics for infective conjunctivitis in children.

### Three-day courses of antibiotics for uncomplicated urinary tract infection

According to PHE guidance on managing common infections in primary care, a 3-day course of antibiotics is sufficient for acute symptomatic UTI in most women with no fever or flank pain who are not pregnant. Nitrofurantoin is recommended first-line for people with an estimated glomerular filtration rate (eGFR) over 45 ml/min because antibiotic resistance and E. coli bacteraemia in the community are increasing. If eGFR is between 30 and 45 ml/min, nitrofurantoin
should be used only if drug resistance is a problem and there is no alternative (see the September 2014 edition of Drug Safety Update for more information). If nitrofurantoin is unsuitable or if eGFR is less than 45 ml/min, pivmecillinam is recommended as the alternative first-line option. Trimethoprim is only recommended if there is a low risk of resistance, depending on local resistance patterns. PHE recommends that risk factors for resistance should be considered and culture and sensitivity testing should be performed if first-line treatment for UTI fails. PHE has produced guidance for primary care on diagnosing UTI and understanding culture results.

The ESPAUR report 2016 found that there was wide variation in the rates of resistance to trimethoprim (and other antibiotics) across England. In Gram-negative UTI, trimethoprim resistance ranges from 16.3% to 66.7% across clinical commissioning groups (CCGs). This may be related to variation in sending urine samples for laboratory testing. However, the report states that 86% of CCGs have resistance rates greater than 25%, highlighting that trimethoprim can no longer be advised as the first-line empiric antibiotic treatment for UTIs in England.

More information on antimicrobial stewardship and managing infections can be found in NICE’s clinical knowledge summaries, antimicrobial prescribing guidelines, and various guidelines, pathways and quality standards on infections. The Department of Health webpage on antimicrobial resistance includes resources for healthcare professionals to help improve infection prevention and control practices and prescribing.

**Practice examples and shared learning**

There are several NICE shared learning examples relating to antimicrobial stewardship, showing how NICE guidance and standards have been put into practice by some NHS organisations:

- NECS e-learning: antibiotic prescribing and antimicrobial stewardship in primary care.
- Reducing the risk of C. difficile by reviewing the prescribing of high-risk antibiotics.
- Reducing antibiotic prescribing by 15% using NICE respiratory tract illness prescribing guidelines.
- Appropriate antibiotic usage in care homes.

**Prescribing data, metrics or supporting resources**

The selection of metrics to support key therapeutic topics is overseen by the NHS England Medicines Optimisation Intelligence Group, and work is ongoing in this area. At this point, the following metrics have been identified by this group to support this topic.
In April 2015, NHS England launched a national programme to reduce inappropriate antibiotic prescribing, with incentive funding for hospitals and clinical commissioning groups (CCGs). The payments form part of 2 schemes that reward excellence and quality improvement: the Commissioning for Quality and Innovation (CQUIN) and the Quality Premium scheme. For 2016/17, a new CCG improvement and assessment framework was also launched, which includes antimicrobial resistance indicators.

CCG performance against the antimicrobial resistance quality premium and the antimicrobial resistance indicators in the CCG improvement and assessment framework is reported monthly via the NHS England Antibiotic quality premium monitoring dashboard and the national antimicrobial stewardship dashboard on ePACT2.

The Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection (APRHAI), which provides advice to the government on minimising the risk of healthcare associated infections, has agreed antimicrobial prescribing quality measures for primary and secondary care.

Three medicines optimisation key therapeutic topic (MO KTT) prescribing comparators are available:

- Antibacterial items/STAR-PU
- Co-amoxiclav, cephalosporins & quinolones % items
- 3 day courses of antibiotics: ADQ/item.

The Medicines optimisation dashboard, which brings together a range of medicines-related metrics from across sectors, includes the first 2 of these comparators. The medicines optimisation dashboard helps NHS organisations to understand how well their local populations are being supported to optimise medicines use and inform local planning. The dashboard allows NHS organisations to highlight variation in local practice and provoke discussion on the appropriateness of local care. It is not intended as a performance measurement tool and there are no targets. The antibacterial items/STAR-PU comparator and the co-amoxiclav, cephalosporins & quinolones % items comparator, plus additional comparators aligned to the CCG quality premium and the CCG improvement and assessment framework, are also included in the national antimicrobial stewardship dashboard on ePACT2.
Update information

February 2018: This topic was retained for the 2018 update of medicines optimisation: key therapeutic topics. The evidence context has been updated in the light of new guidance and important new evidence.

January 2017: This topic was retained for the 2017 update of medicines optimisation: key therapeutic topics. The focus has been changed to antimicrobial stewardship, and this topic now also includes key information from the 3-day courses of antibiotics for uncomplicated urinary tract infection topic. The evidence context has been updated in the light of new guidance and important new evidence.

About this key therapeutic topic

This document summarises the evidence base on this key therapeutic topic which has been identified to support medicines optimisation. It is not formal NICE guidance.

For information about the process used to develop the Key therapeutic topics, see the integrated process statement.

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