

Antimicrobial stewardship: prescribing antibiotics

Key therapeutic topic

Published: 15 January 2015

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Key points

- Antimicrobial resistance poses a significant global threat to public health, especially because antimicrobials underpin routine medical practice.
- Addressing antimicrobial resistance through improving stewardship is a national medicines optimisation priority that is led by [NHS England](#) and supported by [Public Health England](#) (PHE).
- NICE, in collaboration with PHE, is developing clinical syndrome-specific guidance and advice, which offer evidence-based [antimicrobial prescribing](#) information for all care settings to help slow the development of antimicrobial resistances.
- A national programme to reduce inappropriate antibiotic prescribing is in place through the Commissioning for Quality and Innovation (CQUIN) and the Quality Premium (QP) schemes.
- Antimicrobial resistance features in the [NHS Long Term Plan](#) published in January 2019.
- **Options for local implementation:**
 - Review and, if appropriate, revise 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](#).
 - Optimise current prescribing practice and use implementation techniques to ensure

- – prescribing is in line with NICE [antimicrobial prescribing guidelines](#) or the NICE/PHE [summary of antimicrobial prescribing guidance – managing common infections](#), PHE guidance [Start smart – then focus](#), local trust antimicrobial guidelines and the Antimicrobial Stewardship in Primary Care collaboration [TARGET antibiotics toolkit](#).
- Promote the [Antibiotic Guardian](#) call to action and the [Keep Antibiotics Working campaign](#).

Evidence context

Antimicrobial resistance and stewardship

Antimicrobial resistance poses a significant global threat to public health, especially because antibiotics underpin routine medical practice. In response, the World Health Organization (WHO) has developed a [global action plan on antimicrobial resistance](#). 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 2018](#). This states that the proportions of bacterial species causing bloodstream infections that are resistant to key antibiotics have remained stable over the last 5 years probably because of more effective antimicrobial stewardship. However, the estimated total numbers caused by pathogens resistant to 1 or more key antibiotics has increased from 12,250 in 2013 to 16,504 in 2017, a rise of 35%, in particular those caused by [Escherichia coli](#) (*E. coli*) and [Klebsiella pneumoniae](#) (*K. pneumoniae*). The [2018 ESPAUR report](#) stated that the proportion of *E. coli* bloodstream infections non-susceptible to piperacillin/tazobactam (the most frequently used antibiotic for the treatment of sepsis) increased year on year between 2013 and 2017, from 10.6% to 15.3%. For *K. pneumoniae* bloodstream infections non-susceptible to piperacillin/tazobactam, there was an increase between 2013 and 2017 from 16.4% to 19.4%. The [2016 ESPAUR 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 2018](#), methicillin-resistant

Staphylococcus aureus bloodstream infections continued to decline year on year from 9.5% in 2012/13 to 6.6% in 2017/18 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.

The national antimicrobial prescribing and stewardship competencies for prescribers aim to improve the quality of antimicrobial treatment and stewardship and so reduce the risks of inadequate, inappropriate and ill-effects of treatment. They complement the national generic prescribing competency framework. Regulators, education providers and professional bodies can also use them to inform the development of standards, guidance and training.

The WHO has also identified that improving awareness and understanding of antimicrobial resistance through effective communication, education and training is critical to tackling this issue. NICE has 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 2018 states that almost 58,000 people from 129 countries 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. PHE 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. Addressing antimicrobial resistance through improving stewardship is a national medicines optimisation priority, led by [NHS England](#) and supported by [PHE](#).

A NICE medicines evidence commentary on [prescribing feedback and decision support tools for antibiotic prescribing for respiratory tract infections](#) found that an antimicrobial stewardship intervention (including brief training, prescribing feedback and decision support tools) reduced antibiotic prescribing in primary care for self-limiting respiratory tract infections. This provided an example of where feedback and education can be used to support the national antimicrobial stewardship agenda, as highlighted in the NICE guideline on [systems and processes for effective antimicrobial medicine use](#).

Antibiotic prescribing

The Department of Health and Social Care has commissioned NICE, in collaboration with PHE, to develop clinical syndrome-specific guidance and advice, which offer evidence-based [antimicrobial prescribing](#) information for all care settings to help slow the development of antimicrobial resistances.

To help prevent the development of resistance, it is important to prescribe antibiotics only when they are necessary, and not for self-limiting mild respiratory 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.

NICE recommends that in most cases, consideration should be given to a no, or [back-up \(delayed\) antibiotic strategy](#) for people with acute [self-limiting upper respiratory tract infections](#), such as in people with [acute cough](#), [sore throat](#) and [otitis media](#). An immediate antibiotic prescription is still appropriate in some situations (see the individual guidelines for further information).

NICE recommends that people should be given supporting information about antibiotic strategies, infection severity and usual duration, such as the PHE leaflet on [managing your infection](#). NICE has also published a suite of antimicrobial prescribing guidelines on [urinary tract infections \(UTIs\)](#) and decision aids for [lower](#) and [recurrent UTI](#) to help healthcare professionals discuss the antimicrobial prescribing options. PHE has produced guidance for primary care on [diagnosing UTI and understanding culture results](#).

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).

The Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection (APRHAI) 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 to 72 hours. A study of Start smart – then focus, which was discussed in NICE's 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 hospital antibiotic policies 'focus' by reviewing the ongoing need for antibiotics after a couple of days, as recommended.

Safety issues with fluoroquinolones and quinolones

A number of safety issues with fluoroquinolone and quinolone antibiotics have been raised. For example, in the November 2018 edition of the Drug Safety Update, the Medicines and Healthcare products Regulatory Agency (MHRA) highlighted a small increased risk of aortic aneurysm and dissection with systemic and inhaled fluoroquinolones, and recommended caution and advice for prescribing in people with a high risk.

In the March 2019 edition of the Drug Safety Update, the MHRA highlighted new restrictions and precautions for use with the fluoroquinolones following an EU-wide review into the safety of these antibiotics. The review found that very rarely, people having treatment with these antibiotics by mouth, injection or inhalation reported long-lasting and disabling side effects, mainly involving muscles, tendons, joints and the nervous system.

Following on from the review, the marketing authorisations of the fluoroquinolone antibiotics ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin were restricted. They should not be used:

- to treat self-limiting infections, or infections that are not severe
- to treat non-bacterial conditions

- to treat some mild to moderate infections (such as acute exacerbation of chronic bronchitis and chronic obstructive pulmonary disease; see [revised indications in the summary of product characteristics](#)), unless other antibiotics that are commonly recommended for these infections are not appropriate.

Ciprofloxacin or levofloxacin should no longer be prescribed for uncomplicated cystitis unless other antibiotics that are commonly recommended are not appropriate. The marketing authorisation for the quinolone antibiotic nalidixic acid has been cancelled because it was authorised for UTIs, which are no longer permitted indications.

Fluoroquinolone antibiotics should be avoided when treating infections in people who have previously experienced serious adverse events with fluoroquinolone or quinolone antibiotics. They should be used with caution especially in people who are at higher risk of tendon injury, such as people older than 60 years, or people with kidney problems or who have had an organ transplantation. Using a fluoroquinolone together with a corticosteroid should be avoided because the risk of fluoroquinolone-induced tendinitis and tendon rupture may be exacerbated. [Prescribing information for healthcare professionals and information for patients](#) will be updated accordingly.

The MHRA recommends that people should be advised to stop treatment with fluoroquinolone antibiotics at the first signs of a serious adverse reaction, such as tendinitis or tendon rupture, muscle pain, muscle weakness, joint pain, joint swelling, peripheral neuropathy, and central nervous system effects, and to contact their doctor immediately for further advice. The MHRA has produced a [patient sheet](#) to help healthcare professionals to discuss the new measures and actions patients should take.

C. difficile infection

Addressing healthcare-associated *C. difficile* infection remains a key issue on which NHS organisations have been mandated to implement national guidance. PHE guidance on the [management and treatment of C. difficile infection](#) recommends a suitable approach. This guideline is currently being updated. NICE's medicines evidence commentary on [comparative efficacy of antibiotics for C. difficile infection](#) discusses a systematic review and meta-analysis considering the efficacy of antibiotics for adults with this infection.

The Department of Health and PHE report on [C. 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). NICE guidance on [antimicrobial stewardship](#) recommends that 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 where appropriate.

A NICE evidence summary on [C. difficile infection: risk with broad-spectrum antibiotics](#) reviews the evidence on this issue. 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.

A NICE medicines evidence commentary on the [risk of methicillin-resistant Staphylococcus aureus \(MRSA\) and C. difficile in people with documented 'penicillin allergy'](#) found that there was an increased risk of MRSA and *C. difficile* infection in people with documented 'penicillin allergy' and suggested that the increased risk was brought about by the increased use of antibiotics selected as an alternative to beta-lactams. This highlighted the importance of ensuring that only 'true' penicillin allergies are documented in line with the NICE guideline on [drug allergy: diagnosis and management](#).

Antimicrobial prescribing patterns

The [ESPAUR report 2018](#) 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.

The [ESPAUR report 2018](#) reports that use of broad-spectrum antibiotics continues to decline. The

mean proportion of co-amoxiclav, cephalosporins and quinolones as a proportion of all antibiotic items prescribed in primary care reduced from 10.7% to 8.9% between 2015 and 2017. Until 2015, hospitals were continuing to increase their use of the antibiotics of last resort (piperacillin/tazobactam, carbapenems and colistin). However, in 2017/18, 23%, 75% and 45% of 152 NHS acute trusts met their objectives to reduce total antibiotic, piperacillin/tazobactam and carbapenem consumption, respectively. The global shortage of piperacillin/tazobactam in 2017 has influenced the fall in consumption of this particular antibiotic but the overall, general downward trend is an encouraging step towards improving antibiotic stewardship 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.

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 [antibiotic use](#) and [infections](#). The Department of Health and Social Care 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 case studies](#) 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.](#)

Prescribing data, metrics or supporting resources

At this point, the following metrics have been identified 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 \(QP\) scheme](#). Current CQUIN performance is reported monthly via the PHE [Fingertips AMR Portal](#).

CCG performance against the antimicrobial resistance QP scheme 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 [prescribing comparators](#) are available:

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

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

Update information

September 2019: This topic was retained for the 2019 rapid update of medicines optimisation: key therapeutic topics. Minor editorial changes have been completed, links to new medicines evidence

commentaries have been added and the section on safety issues with fluoroquinolones and quinolones has been updated to reflect Medicines and Healthcare products Regulatory Agency (MHRA) advice.

About this key therapeutic topic

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

ISBN: 978-1-4731-0942-1